Louisiana State University
LSU Digital Commons

LSU Historical Dissertations and Theses | Graduate School

1996

# Conditioning the Auditory System With Continuous Versus Interrupted Noise of Equal Acoustic Energy: Is Either Exposure More Protective?

Ruth Ann Skellett
*Louisiana State University and Agricultural & Mechanical College*

Follow this and additional works at: https://digitalcommons.lsu.edu/gradschool_disstheses

Recommended Citation
Skellett, Ruth Ann, "Conditioning the Auditory System With Continuous Versus Interrupted Noise of Equal Acoustic Energy: Is Either Exposure More Protective?" (1996). *LSU Historical Dissertations and Theses*. 6280.
https://digitalcommons.lsu.edu/gradschool_disstheses/6280

This Dissertation is brought to you for free and open access by the Graduate School at LSU Digital Commons. It has been accepted for inclusion in LSU Historical Dissertations and Theses by an authorized administrator of LSU Digital Commons. For more information, please contact gradetd@lsu.edu.

## INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

**The quality of this reproduction is dependent upon the quality of the copy submitted.** Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

UMI

A Bell & Howell Information Company
300 North Zeeb Road. Ann Arbor. MI 48106-1346 USA
313/761-4700 800/521-0600

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CONDITIONING THE AUDITORY SYSTEM WITH CONTINUOUS VERSUS INTERRUPTED NOISE OF EQUAL ACOUSTIC ENERGY: IS EITHER EXPOSURE MORE PROTECTIVE?

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

in

The Department of Communication Sciences and Disorders

by
Ruth Ann Skellett
B.S., Florida Institute of Technology, 1987
M.S., Medical College of Virginia, 1990
August 1996

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

UMI Number: 9706363

UMI Microform 9706363
Copyright 1996, by UMI Company. All rights reserved.

This microform edition is protected against unauthorized
copying under Title 17, United States Code.

UMI
300 North Zeeb Road
Ann Arbor, MI 48103

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

To Mom and Dad...

Your love and support has guided me along every path that I have decided to walk and has encouraged me to continue even when obstacles surfaced. I dedicate this work to you because you are not only two very special parents, but also two very special friends. I love you.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**ACKNOWLEDGMENTS**

I would like to thank my committee members, John K. Cullen, Jr., Ph.D., Richard P. Bobbin, Ph.D., M. Jane Collins, Ph.D., Janna Oetting, Ph.D., George Strain, Ph.D., and Denny LeCompte, Ph.D. for their help and encouragement during this final leg of my journey towards the completion of my doctoral degree. I am especially grateful to my advisor, Dr. Jack Cullen, for his unending support and for the occasional kick in the #@! I needed to get over the writer's block that I sometimes experienced.

I owe much of my success to Dr. Richard P. Bobbin who, approximately four years ago, gave me the opportunity to work in his laboratory and then allowed me to become a member of his successful laboratory team. Dr. Bobbin has helped me strive to become a better research scientist by providing me with challenges on a daily basis. And, oh, how I love to play twenty questions! I am grateful for his friendship and all of the support that he has given me over the years.

Special thanks to Maureen Fallon for her help with the surgical procedures that were imperative to the success of this experiment and all of the beautiful graphs that were included within this dissertation. She has played a vital role in all that I have been involved in during my four years in the lab and for this, I am deeply grateful. I would also like to thank Maureen, and her husband, Jim



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Bolongaro, for their friendship and for their support when the going got rough.

Thank you to everyone at Kresge Hearing Research Laboratory of the South. I would especially like to thank all of my co-workers in the lab, past and present, for being so supportive. This list includes Latasha Bright, Clare Cahalan, Julie Campbell, Chu Chen, Sally Chu, Don Fraser, Kathy Klotz, Sharon Kujawa, Chris LeBlanc, Elaine McDonald, Anastas Nenov, David Owens, Steven Owens, and Sharon Parker. I am especially grateful to Latasha and Julie for their help with my dissertation. Things went well until we discovered the 50% paper (Ha Ha).

To my family: Mom, Dad, Bob (and kids), Lisa (and family), and Mark... you have always been there for me through everything I've attempted and accomplished throughout my life and my entire college career (don't tell anybody, but I think that covers a 16 year period). I love you.

Finally, special thanks to my best friend, Ann Bain, for hanging with me for all of these years even after we finished Dr. Webster's anatomy class (you and you!). You were the best lab partner and are the best friend that anyone could ask for. I appreciate all of the support that you have provided me over the years (AT&T and MCI thank you too).



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**TABLE OF CONTENTS**


DEDICATION ..... ii

ACKNOWLEDGEMENTS ..... iii

LIST OF TABLES ..... vii

LIST OF FIGURES ..... xi

ABSTRACT ..... xiii

CHAPTER

1 INTRODUCTION ..... 1

2 BACKGROUND ..... 4
2.1 Noise Exposure - General Overview ..... 4
2.2 Protection Against Noise Trauma by Prior Sound Conditioning ..... 9
2.3 Mechanisms Responsible for Protection .. 25
2.4 Distortion-product Otoacoustic Emissions (DPOAEs) ..... 32
2.5 The Equal Energy Hypotheses ..... 34

3 METHODS ..... 42
3.1 Subjects ..... 42
3.2 Noise Generation and Exposure Methods .. 42
3.2.1 Noise Exposure Facility ..... 42
3.2.2 Noise Generation and Calibration Procedures ..... 43
3.3 General Surgical Methods ..... 47
3.4 DPOAE Generation and Calibration Procedures ..... 48
3.5 DPOAE Input-Output Measurements ..... 49
3.6 Experimental Design and Noise Exposure Protocols ..... 51
3.7 Data Management and Analysis ..... 54

4 RESULTS ..... 56
4.1 Effects of the Sound Conditioning Exposure Protocols on DPOAE Responses . 56
4.2 Effects of the Traumatizing Noise Exposure on the DPOAE Responses of Unconditioned and Sound Conditioned Animals ..... 66

5 DISCUSSION ..... 91
5.1 Baseline DPOAE Responses ..... 93
5.2 Effects of Sound Conditioning on DPOAE Responses ..... 95
5.2.1 Continuous Sound Conditioning ... 95
5.2.2 Interrupted Sound Conditioning .. 106




Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

5.2.3 Comparison of the Effects of the Two Sound Conditioning Protocols - Testing the Validity of the EEH ..... 115
5.3 Effects of the Traumatizing Noise Exposure on DPOAE Responses ..... 119
5.3.1 Unconditioned Animals (Blast Only Group) ..... 119
5.3.2 Sound Conditioned Animals ..... 123
5.3.2.1 Continuous Sound Conditioning ..... 123
5.3.2.2 Interrupted Sound Conditioning ..... 127
5.3.3 Comparison of the Effects of the Traumatizing Noise Exposure on the DPOAE Responses of Unconditioned and Sound Conditioned Animals -- Did Sound Conditioning Provide Protection? ..... 130
5.3.3.1 Did Continuous Sound Conditioning Provide Protection Against the Damaging Effects of the Traumatizing Noise Exposure ..... 131
5.3.3.2 Did Interrupted Sound Conditioning Provide Protection Against the Damaging Effects of the Traumatizing Noise Exposure ..... 137
5.3.4 Comparison of the Effects of the Traumatizing Noise Exposure on the DPOAE Responses of Animals Conditioned with Continuous vs. Interrupted Moderate-level Noise -- Is Either Sound Conditioning Protocol More Protective? ..... 143

6 SUMMARY AND CONCLUSIONS ..... 151

REFERENCES ..... 155

APPENDIXES

A INDIVIDUAL ANIMAL DPOAE AMPLITUDE DATA .... 170

B MEAN DPOAE AMPLITUDE DATA ..... 198

VITA ..... 207



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

## LIST OF TABLES


1. Primary Tones and Corresponding DPOAEs (measured in Hz) ..... 50

2. Experimental Design ..... 55

3. Three-way ANOVA Table - Analysis of the Effects of the Sound Conditioning Exposure Protocols on DPOAE Responses ..... 67

4a. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 707 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 68

4b. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 1000 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 69

4c. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 1414 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 70

4d. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 2000 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 71

4e. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 2828 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 72

4f. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 4000 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 73

4g. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 5656 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 75




Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

4h. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Intensity Found for DPOAE Responses when $f_2$ = 8000 Hz for the Aged Normal (AGE), Continuous (CON), and Interrupted (INT) Conditioning Groups ..... 77

5. Three-way ANOVA Table - Analysis of the Effects of the Traumatizing Noise Exposure on the DPOAE Responses of Unconditioned and Sound Conditioned Animals ..... 88

6. Summary of the Tukey Multiple Comparison Test Results for the Main Effect of Group Found for DPOAE Responses when Pooling the Data across Frequency and Intensity for the Blast Only (BLA), Continuous Conditioning then Blast (C&B), and Interrupted Conditioning then Blast (I&B) Groups ..... 89

7. Summary of the Tukey Multiple Comparison Test Results for the Group x Frequency Interaction Found for DPOAE Responses when Pooling the Data across Intensity for the Blast Only (BLA), Continuous Conditioning then Blast (C&B), and Interrupted Conditioning then Blast (I&B) Groups ..... 90

8. Mean Amplitude Difference Data (in dB) Between the Aged Normal Group and the Continuous Conditioning Group ..... 96

9. Mean Amplitude Difference Data (in dB) Between the Aged Normal Group and the Interrupted Conditioning Group ..... 107

10. Mean Amplitude Difference Data (in dB) Between the Aged Normal Group and the Blast Only Group ..... 120

11. Mean Amplitude Difference Data (in dB) Between the Aged Normal Group and the Continuous Conditioning then Blast Group ..... 125

12. Mean Amplitude Difference Data (in dB) Between the Aged Normal Group and the Interrupted Conditioning then Blast Group ..... 128

13. Mean Amplitude Difference Data (in dB) Between the Blast Only Group and the Continuous Conditioning then Blast Group ..... 132

14. Mean Amplitude Difference Data (in dB) Between the Blast Only Group and the Interrupted Conditioning then Blast Group ..... 138



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

15. Mean Amplitude Difference Data (in dB) Between the Interrupted Conditioning then Blast Group and the Continuous Conditioning then Blast Group ..... 145

16a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=707 Hz ..... 198

16b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=707 Hz ..... 198

17a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=1000 Hz ..... 199

17b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=1000 Hz ..... 199

18a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=1414 Hz ..... 200

18b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=1414 Hz ..... 200

19a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=2000 Hz ..... 201

19b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=2000 Hz ..... 201

20a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=2828 Hz ..... 202

20b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=2828 Hz ..... 202



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

21a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=4000 Hz ..... 203

21b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=4000 Hz ..... 203

22a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=5656 Hz ..... 204

22b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=5656 Hz ..... 204

23a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=8000 Hz ..... 205

23b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=8000 Hz ..... 205

24a. Mean DPOAE Amplitude Data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=11312 Hz ..... 206

24b. Mean DPOAE Amplitude Data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=11312 Hz ..... 206



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

## LIST OF FIGURES


1. Spectral characteristics of the continuous conditioning noise (89 dB SPL; top), the interrupted conditioning noise (95 dB SPL; middle), and the traumatizing noise (105 dB SPL; bottom) exposures ..... 46

2a. The effect of sound conditioning on DPOAE responses at $f_2$ = 707 Hz ..... 57

2b. The effect of sound conditioning on DPOAE responses at $f_2$ = 1000 Hz ..... 58

2c. The effect of sound conditioning on DPOAE responses at $f_2$ = 1414 Hz ..... 59

2d. The effect of sound conditioning on DPOAE responses at $f_2$ = 2000 Hz ..... 60

2e. The effect of sound conditioning on DPOAE responses at $f_2$ = 2828 Hz ..... 61

2f. The effect of sound conditioning on DPOAE responses at $f_2$ = 4000 Hz ..... 62

2g. The effect of sound conditioning on DPOAE responses at $f_2$ = 5656 Hz ..... 63

2h. The effect of sound conditioning on DPOAE responses at $f_2$ = 8000 Hz ..... 64

2i. The effect of sound conditioning on DPOAE responses at $f_2$ = 11312 Hz ..... 65

3a. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 707 Hz ..... 79

3b. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 1000 Hz ..... 80

3c. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 1414 Hz ..... 81

3d. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 2000 Hz ..... 82

3e. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 2828 Hz ..... 83




Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

3f. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 4000 Hz ..... 84

3g. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 5656 Hz ..... 85

3h. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 8000 Hz ..... 86

3i. The effect of the traumatizing exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 11312 Hz ..... 87

4. The effect of continuous sound conditioning on normal DPOAE responses ..... 97

5. The effect of interrupted sound conditioning on normal DPOAE responses ..... 108

6. The effect of the traumatizing noise on normal DPOAE responses ..... 121

7. The effect of the continuous conditioning/ traumatizing noise exposure combination on normal DPOAE responses ..... 126

8. The effect of the interrupted conditioning/ traumatizing noise exposure combination on normal DPOAE responses ..... 129

9. Comparison of the effect of the traumatizing noise on the DPOAE responses of the unconditioned vs. the continuous sound conditioned groups ..... 133

10. Comparison of the effect of the traumatizing noise on the DPOAE responses of the unconditioned vs. the interrupted sound conditioned groups ..... 139

11. Comparison of the effects of the traumatizing noise exposure on the DPOAE responses of animals conditioned with continuous vs. interrupted moderate-level noise ..... 146



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**ABSTRACT**

Prior exposure to moderate-level acoustic stimulation (conditioning) can reduce and/or prevent the deleterious effects of subsequent higher level exposures (Canlon et al., 1988; Campo et al., 1991). Both continuous and interrupted schedules of moderate-level noise have been used as conditioning exposures, and both schedules have been effective in providing protection against subsequent noise trauma. However, there is evidence to suggest that continuous noise exposures are more damaging to the cochlea than interrupted exposures of equal acoustic energy (Bohne et al., 1985, 1987), and moderate-level continuous and interrupted noise exposures differ in the pattern of auditory sensitivity change that they produce over time (Carder and Miller, 1972; Miller et al., 1963). A question arises as to whether there are differences in the amount of protection afforded by prior conditioning of the auditory system with moderate-level continuous or interrupted noise.

The purpose of this study was to test the hypothesis that differences exist in the amount of protection provided by prior sound conditioning with continuous vs. interrupted, moderate-level noise. Differences were determined by monitoring the changes that occurred in distortion product otoacoustic emission amplitude growth functions subsequent to a traumatizing noise exposure in guinea pigs which had been conditioned with either continuous or interrupted noise of equal acoustic energy.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Results suggest that there are significant differences in the degree of protection provided by prior sound conditioning with the continuous and interrupted schedules of moderate-level noise used in this study. Specifically, the interrupted conditioning protocol appears to afford some degree of protection against the damaging effects of the traumatizing noise exposure. However, the frequency region that is protected is limited to frequencies above the noise exposure band. Conversely, there is a lack of any consistent and sizable protective effect found across the entire test frequency range for the continuous sound conditioning protocol. Given the disparate findings of this and other studies, it appears that the protective role of sound conditioning with moderate-level noise is not a straightforward phenomenon and is highly dependent on the noise exposure conditions, animal species, and response measurements studied.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CHAPTER 1

## INTRODUCTION

Noise-induced hearing loss is a public health problem that has been listed among the top ten work-related diseases/injuries by the Center for Disease Control (1983). The Environmental Protection Agency (1981) estimated that nine million Americans were exposed to levels of noise at their work place which put them at risk for noise-induced hearing loss. In all probability this number has grown larger since that time. However, the existence of large individual differences in susceptibility to noise exposure has not only made it difficult to understand the basic mechanisms of noise-induced hearing loss, but has also made it difficult to effectively implement hearing conservation programs in the workplace.

Not all individuals exposed to similar noise conditions incur equal damage or hearing loss. There are several factors, both nonauditory and auditory, that have been suggested as influences on an individual's susceptibility to noise-induced hearing loss. Nonauditory factors include age (Szanto and Ionescu, 1983; Mills, 1992), gender (Szanto and Ionescu, 1983), eye color (Carlin and McCrosky, 1980; Carter, 1980; Kleinstein et al., 1984; Barrenäs and Lindgren, 1990; Barrenäs and Hellström, 1996), and smoking history (Barone et al., 1987; Prince and Matanoski, 1991). Also, the use of ototoxic drugs (McFadden and Plattsmier, 1983; McFadden, 1986; Gratton et



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

al., 1990) has been shown to exacerbate the effects of noise exposure. Auditory factors include the efficiency or attenuation characteristics of the acoustic reflex (Zakrisson et al., 1980; Borg and Nilsson, 1984; Rodriguez and Gerhardt, 1988;), activation of the medial cochlear efferent system (Cody and Johnstone, 1982; Puel et al., 1988b; Rajan, 1992), and an individual's previous noise exposure history (Miller et al., 1963; Clark et al., 1987).

In recent years, considerable attention has been given to the idea that susceptibility of the auditory system to noise-induced hearing loss may be lessened by an individual's previous history of noise exposure. Prior exposures to moderate-level acoustic stimulation (i.e., conditioning) can reduce (and in some instances prevent) the deleterious effects of subsequent higher level (and usually damaging) exposures (Canlon et al., 1988, 1992; Campo et al., 1991; Henderson et al., 1992; Ryan et al., 1994). Both continuous and interrupted schedules of moderate-level noise have been used as conditioning exposures, and both schedules have been effective in providing protection against subsequent noise trauma.

Under most conditions, prevention of noise-induced hearing loss is best achieved either by controlling the level and duration of the noise exposure or by consistent and proper use of hearing protection. However, there are certain occupational situations wherein either of these alternatives is impractical. In such cases, it would be of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

great benefit to establish a protocol which incorporates the prophylactic use of low-to-moderate level noise for the prevention of noise-induced hearing loss.

It is currently unknown whether there are differences in the amount of protection afforded by prior conditioning of the auditory system with either a moderate-level continuous or interrupted noise exposure schedule. Thus, the purpose of this study is to test the hypothesis that differences exist in the amount of protection provided by prior sound conditioning with continuous versus interrupted moderate-level noise. The results of this study will help determine the better sound conditioning protocol to use in clinical situations and add to the pre-existing body of knowledge concerning this type of protective phenomenon.

The differences in protective effect of the two conditioning schedules were determined by monitoring changes that occur in distortion product otoacoustic emission (DPOAE) amplitude growth functions after a subsequent higher level (traumatizing) exposure in guinea pigs (*Cavia cobaya*) that had been conditioned with either continuous or interrupted noise. Both conditioning exposure schedules had the same total acoustic energy consistent with the Equal Energy Hypothesis (EEH; Eldred et al., 1955). This equal energy requirement was considered important in the design of the study because it yielded noise exposures that differed only in their temporal pattern.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CHAPTER 2

# BACKGROUND

This chapter provides a general overview of the effects of noise on the structure and function of the cochlea, focusing primarily on the effects of continuous vs. interrupted noise exposures. This is followed by an in depth review of the literature discussing the protective role of prior, moderate-level noise exposures (conditioning) against subsequent damaging exposures and the possible physiological mechanisms responsible for this protective phenomenon. Finally, two concepts relevant to the design of this study -- distortion-product otoacoustic emissions (DPOAEs) and the Equal Energy Hypothesis (EEH) -- are discussed.

## 2.1 Noise Exposure - General Overview

Noise exposure induces several alterations in structure and function throughout the cochlea (Saunders et al., 1985, 1991). The outer hair cells (OHCs) represent the cochlear components that are initially and most critically compromised by acoustic overstimulation (Clark and Bohne, 1978). Both mechanical and/or metabolic processes have been suggested as the mechanisms responsible for OHC damage in response to noise exposure (Lim and Dunn, 1979). Mechanically-induced damage usually has a very rapid onset due to extreme movements of the cochlear partition in response to intense sound. Metabolically-induced damage, on the other hand, has a more gradual



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

onset, usually in response to long-term, low-to-moderate level exposures. Cellular processes which are important for energy production, protein synthesis, and ion transport are compromised under conditions of excessive sound stimulation resulting in an eventual lack of cell maintenance and possible cell death.

The magnitude of OHC damage differs depending on the exposure conditions of the noise (i.e., frequency, level, and duration) and appears to be species-specific (Hamernik et al., 1984). In general, low-to-moderate level exposures of short durations result in an increase in the amount of smooth endoplasmic reticulum within OHCs (Engström et al., 1970; Ward and Duvall, 1971) and disorganized proliferation of the subsurface cisternae and Hensen's bodies (Slepecky et al., 1982). These exposure-induced effects appear to be temporary and involved structures return to normal after a sufficient period of recovery. When more severe stress is placed on the auditory system by increasing the intensity and/or duration of the exposure, more permanent structural alterations within the OHCs occur. These include vacuolation or vesiculation of the endoplasmic reticulum (Lim and Dunn, 1979), swelling of the mitochondria (Ward and Duvall, 1971; Lim and Dunn, 1979), an increase in the number of lysosomes just below the basal body (Slepecky et al., 1982), and an increase in lipofuscin granules (Engström and Engström, 1979). Swelling of the OHCs and their nuclei may also take place (Liberman and Kiang,

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

1978). There is an overall increase in the number of missing OHCs under such conditions.

The stereocilia of the hair cells are also affected by acoustic overstimulation in an "exposure-dependent" manner. The array of acoustic injuries to the stereocilia range from floppy, disarrayed, blebbed, and collapsed stereocilia with mild-to-moderate noise exposures to fused, elongated, giant, and missing stereocilia with more intense exposures (Saunders et al., 1985). Noise exposure may also damage the tip links, cross bridges, and rootlets of the stereocilia. Damage to the connections between the stereocilia and the tectorial membrane as well as depolymerization of the stereocilia is often observed.

Another factor that affects the magnitude of hair cell damage is the temporal pattern of the noise exposure. Continuous noise exposure involves signals that have a relatively long "on"-time and a peak sound pressure level (SPL) which is not significantly different from the average SPL. An interrupted exposure is similar to a continuous exposure; however it involves long periods (at least several hours) of effective quiet. Many investigations have focused on the histological changes associated with continuous and interrupted exposure schedules to help determine if the rest (quiet) periods within the interrupted exposure act to minimize hair cell damage (Bohne et al., 1985, 1987; Fredelius and Wersäll, 1992). The results of these studies suggest that continuous noise

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

exposure is more damaging to the cochlea than an interrupted exposure of equal energy.

Continuous and interrupted noise exposures also differ in the pattern of sensitivity change that they produce over time. Continuous or prolonged noise exposure results in a decrease in auditory sensitivity that grows over the first 18-24 hours of the exposure and then stabilizes or reaches a plateau as the exposure continues. This pattern of sensitivity change is referred to in the behavioral literature as an asymptotic threshold shift (ATS; Carder and Miller, 1972). ATS depends upon both the level and frequency of the exposure. The level of the shift at asymptote increases by 1.6-1.7 dB for every 1-dB increase in noise above a certain level (Mills, 1973a,b). This "certain" level depends upon the octave band of noise used to expose the animals and the acoustic characteristics of the animal's external ear canal. Once the asymptotic level of shift is reached, the decay of threshold shift after removal from the noise is exponential with time and its course is independent of the duration of exposure.

Several investigators have studied the progression of threshold shifts with long-duration continuous exposures [chinchillas (Carder and Miller, 1972; Mills, 1976; Bohne and Clark, 1982; Clark and Bohne, 1987); monkeys (Moody et al., 1976); guinea pigs (Syka and Popelar, 1980); and humans (Melnick, 1976)]. Clark and Bohne (1987) have shown that the level of ATS remains stable for exposure durations

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

lasting as long as three years. However, this "stable" result is somewhat confusing given the existing anatomical and permanent threshold shift (PTS) data. Both anatomical and PTS data suggest that there is a direct relationship between exposure duration and the amount of cochlear damage and PTS (i.e., with increased duration there is an increase in cochlear damage and PTS; Bohne and Clark, 1982). In Clark and Bohne's study (1987), when the animals were removed from the noise for a 1-2 week period during the third year of exposure, 5-20 dB of recovery occurred at all test frequencies. This indicates that ATS may set an upper limit on the amount of PTS resulting from a continuous exposure of infinite duration.

Interrupted noise exposure, on the other hand, results in an initial decrease in auditory sensitivity during the first few days of exposure, followed by a return towards baseline (or pre-exposure levels) on subsequent days of exposure. Miller et al. (1963) were first to suggest that repeated exposures to low-to- moderate level acoustic stimuli might result in less threshold shift over time. In their experiment, cats were exposed to a broad band noise (BBN) with an overall level of 115 dB SPL for 7.5 minutes per day for 16 days. The maximum threshold shift measured behaviorally at 4 kHz (approximately 40 dB) occurred after the second exposure but then decreased to approximately 15 dB by the fifth exposure, and remained at this value for the rest of the experiment. Since the time of this initial

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

report, others have demonstrated the development of substantially less threshold shift with repeated exposures to different schedules of interrupted noise using behavioral (Clark et al., 1987), physiological (Sinex et al., 1987; Byrne et al., 1988; Subramaniam, 1991a,b; Boettcher et al., 1992) and distortion product otoacoustic emission (DPOAE; Subramaniam et al., 1994a,b) measures. This progressive resistance to threshold shift caused by repeated exposures to a conditioning noise interspersed with periods of rest is known as "toughening". Toughening has been demonstrated in many species including cat (Miller et al., 1963), chinchilla (Clark et al., 1987; Sinex et al., 1987; Henderson et al., 1992; Subramaniam et al., 1991a,b, 1994a,b), rabbit, (Franklin et al., 1991), and humans (Ward, 1970; Miyakita et al., 1992).

**2.2 Protection Against Noise Trauma by Prior Sound-Conditioning**

In recent years, considerable attention has been given to the idea that susceptibility of the auditory system to noise-induced hearing loss may be decreased depending upon a subject's previous history of noise exposure. Prior exposures to moderate level acoustic stimulation (i.e., conditioning) can reduce (and in some instances prevent) the deleterious effects of subsequent higher level (and usually damaging) exposures (Canlon et al., 1988, 1992; Campo et al., 1991; Henderson et al., 1992; Ryan et al., 1994; Canlon and Fransson, 1995). Both continuous and interrupted schedules of moderate-level noise exposure have

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

been used as conditioning exposures and both have been effective in providing protection against subsequent traumatizing noise.

Canlon et al. (1988) were first to demonstrate that protection could be afforded by conditioning the guinea pig auditory system with moderate-level stimulation. They showed that prior exposure of guinea pigs to a 1 kHz pure-tone at 81 dB SPL presented continuously for 24 days reduced the damaging effects of a second traumatizing exposure (1 kHz pure-tone at 105 db SPL for 72 hours). The conditioned group of animals exhibited less TTS and PTS than a group of control animals exposed to only the higher level tone. Ninety minutes after the 3-day exposure to the 105 dB SPL 1 kHz tone, both groups had elevated auditory brainstem response (ABR) thresholds at all test frequencies. However, the amount of threshold shift demonstrated by the control group ranged from 33-53 dB across frequency while the conditioned group showed only an 8-40 dB shift. After an 8-week recovery period, ABR thresholds measured in the conditioned group returned to pre-exposure values, while the control group continued to show residual threshold shifts of 14-35 dB depending on test frequency. Thus, the low-level conditioning exposure provided protection against PTS from a higher level exposure at the same frequency.

Campo et al. (1991) replicated the results of Canlon et al. (1988); however, they used chinchillas that were

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

deafened in one ear as their experimental animal and a conditioning exposure more typical of that found in an industrial workplace. The conditioned group of chinchillas was exposed to a 95 dB SPL octave band noise centered at 0.5 kHz for 6 hours a day (6 hours "on"/18 hours "off") for 10 consecutive days. This interrupted schedule of noise exposure resulted in a gradual reduction in the amount of threshold shift over the course of the 10-day exposure. This result was consistent with earlier findings demonstrating toughening of the auditory system (Clark et al., 1987). The animals were then allowed to recover in a quiet environment for 5 days before being exposed to the traumatic exposure (the same spectrum of noise presented continuously at 106 dB SPL for 48 hours). The recovery period was incorporated into the experimental paradigm to ensure that any shift in hearing threshold which might have occurred during the conditioning noise was eliminated and pre-exposure levels retained. The control group of chinchillas was exposed only to the traumatic exposure. Hearing thresholds determined using evoked potential recordings were measured for test frequencies of 0.5- to 16 kHz (in one octave steps) in both groups of animals immediately upon removal from the traumatic noise and then 24 hours, 5 days, and 4 weeks post-exposure. Animals in the control group consistently showed greater threshold shifts than the animals previously conditioned with the interrupted moderate-level noise each time evoked potential

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

thresholds were measured. The final threshold measurement taken 4 weeks post-exposure revealed that the control group experienced 10-20 dB more PTS than the conditioned group at frequencies between 0.5- and 4 kHz. The difference in the amount of PTS between the two groups was statistically significant.

Canlon et al. (1992) tested the persistence of the conditioning effect using rabbits as their animal model. Rabbits were exposed to a 79 dB SPL band of noise (2-7 kHz) for 256 hours. These rabbits were then maintained in a quiet environment for either 2 weeks or 1 month prior to being exposed to a high intensity noise (2 - 4 kHz, 131 dB SPL for 15 minutes). Control rabbits were exposed only to the damaging noise. ABR thresholds measured 3 weeks after the 131 dB SPL exposure showed that the conditioned group acquired 10 - 25 dB less threshold shift than the control group between 0.5- and 4 kHz. Group thresholds did not differ in the 6.3- to 20 kHz region. Therefore, the results suggested that the protective effect of the moderate-level conditioning noise exposure is relatively long-lasting.

Miyakita et al. (1992) investigated whether human subjects could also be protected from the effects of noise trauma by prior sound conditioning with a low-level acoustic stimulus. Normal hearing teenagers with a mean age of 13.5 years (range: 12-16 years) were exposed to 70 dB SPL (A-scale) music for 6 hours per day for 9

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

consecutive days (conditioning exposure). The high-level noise exposure was a 105 dB SPL, ⅓ octave noise band centered at 2 kHz presented for 10 minutes. Hearing thresholds were determined behaviorally by a computerized, sweep-frequency (Bekesy-type) audiometer in the frequency range 0.8- to 8.0 kHz. During the 9-day training period, the subjects were exposed to the music for 6 hours per day. Thresholds were monitored each day (just before and just after exposure) to measure the effects of the music on hearing thresholds. On days 1, 3, 5, 7, and 9 of this period, subjects were exposed to the 105 dB SPL noise for 10 minutes following the 6-hour conditioning exposure and subsequent hearing test. Thresholds were again monitored after the traumatic exposure and the amount of TTS induced by this exposure was determined. Results showed that after 5 days of conditioning, significant decreases in TTS were observed in the 3-3.5 kHz frequency range. As the training continued, the frequency range in which significant reductions in TTS were found increased to 2-5 kHz. However, the TTS reductions observed under the experimental conditions used in this study were not persistent. When subjects were tested 5 days after the training period, the amount of TTS measured after the traumatic exposure was not statistically different from the pre-conditioning baseline threshold shift values.

The duration of the conditioning exposures used by Canlon et al. (1988) and Campo et al. (1991) was relatively

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

long. Subramaniam et al. (1993a) were interested in determining the length of the conditioning exposure required to provide the protective effect and if the amount of protection was dependent upon the number or length of conditioning exposures. Three groups of chinchillas (deafened in one ear) were exposed to a 95 dB SPL octave band noise centered at 0.5 kHz for either: (1) 6 hours and then allowed to recover for 9 days before repeating the same exposure; (2) 6 hours per day for 10 consecutive days; or (3) 6 hours per day for 20 consecutive days. Each group was allowed to recover for 5 days after the last conditioning exposure and then exposed to the same spectrum at 106 dB SPL for 48 hours. A control group was exposed only to the higher level noise. Hearing thresholds determined using evoked potential recordings were measured 4 weeks post-exposure to the 106 dB SPL noise. All three groups of conditioned animals incurred significantly less PTS than the control group at test frequencies between 0.5- and 2 kHz. Animals conditioned over 10 consecutive days showed greater protection from hearing loss over a wider frequency range than the other two conditioned groups; however, this difference was not significant. Interestingly, although all conditioned groups had significantly less PTS than the control group, all groups had approximately the same amount of OHC loss. The authors concluded that a single moderate-level conditioning exposure might possibly be sufficient to trigger a

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

protection process against the damaging effects of a subsequent higher level exposure. However, additional exposures (up to 10 days) were required to increase the protective effect. Further increase in the number of conditioning exposures (20 days) became less effective in preventing hearing loss.

The traumatic exposures used in the studies mentioned thus far have been restricted to continuous noise exposures with intensities of ≤ 106 dB SPL. However, since impulse noise is common to many industrial worksites, military operations, and recreational activities, Henselman et al. (1994) were interested in determining whether conditioning could protect the auditory system against damage resulting from subsequent exposure to high-level impulse noise. An experimental group consisted of seven monaurally deafened chinchillas which were first exposed to a conditioning noise - an octave band noise centered at 0.5 kHz at 95 dB SPL for 6 hours per day for 10 successive days. After a 5-day recovery period from the conditioning exposure, these animals were then exposed to the impulse noise which had peak levels of 150 dB SPL. The impulses were presented using a "salvo" exposure, i.e., the temporal spacing of the impulses consisted of a series of 50 pairs of impulses presented 50 ms apart with 1000 ms between the onset of each pair. The total duration of the exposure was approximately one minute. The control group consisted of 14 monaurally deafened chinchillas which were exposed only

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

to the impulse noise. Hearing thresholds, determined using evoked potential recordings, were measured for test frequencies of 0.5- to 16 kHz (in one octave steps) in both groups of animals 15 minutes, 24 hours, 10 days, and 4 weeks post-traumatic exposure. At all times, the experimental group demonstrated considerably lower threshold shifts than the control group. In fact, there were statistically significant differences in the amount of PTS (measured 4 weeks post-exposure) between both groups at all frequencies tested. Histological findings also revealed significant differences in the amount of inner and outer hair cell loss between the conditioned group of animals and the control animals. Thus, the results of this study support the notion that prior exposure to a low-to-moderate level conditioning noise is an effective means of alleviating the hazardous effects of high level impulse noise.

Canlon and Fransson (1995) were interested in distinguishing between inner and outer hair cell damage in sound conditioned animals that were subsequently exposed to a high-level tone versus animals exposed to only the latter traumatic exposure. The conditioning and traumatic exposures were the same as that used originally by Canlon et al. (1988), i.e., an 81 dB SPL 1 kHz pure tone presented continuously for 24 days and a 105 dB SPL 1 kHz pure tone presented continuously for 3 days. Distortion product otoacoustic emissions (DPOAEs) were chosen for study since

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

they are believed to specifically reflect the functional activity of the outer hair cells (Siegel and Kim, 1982). Five pigmented guinea pigs were first studied to determine the effects of the conditioning exposure. DPOAE input-output functions were measured for the $2f_1$-$f_2$ DPOAE frequencies of 1.75-, 2.1-, 2.8-, and 3.5 kHz before sound conditioning, and on days 1, 5, 10, 15, and 24 during the low-level, long term exposure. Results showed that minor amplitude alterations did occur at DPOAE frequencies 1.75-, 2.1-, and 2.8 kHz on days 1, 5, and 10 for some (but not all) animals. However, by days 15 and 24 of the conditioning exposure, amplitudes were similar to pre-exposure values in all cases. In addition, auditory brainstem response thresholds at 1.0- and 2.0 kHz were not affected at any time during sound conditioning. The analysis of surface preparations of the organ of Corti after a 14 or 30 day rest from the low-level exposure did not reveal any significant hair cell loss induced by the sound conditioning. Thus, Canlon and Fransson (1995) concluded that their sound conditioning paradigm did not cause any significant functional or morphological alterations to the cochlea.

Next, Canlon and Fransson (1995) investigated the effect of the traumatic exposure (1 kHz, 105 dB SPL, 3 days) on a group of sound conditioned guinea pigs and a control group of animals exposed only to the high-level tone. DPOAE input-output functions were measured for the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$2f_1$-$f_2$ DPOAE frequencies of 1.75-, 2.1-, 2.8-, 3.5-, 4.4-, and 5.6 kHz for both groups of animals 4 weeks post-traumatizing exposure. Results showed that statistically significant reductions were not found when comparing the DPOAE input-output functions of the sound conditioned group to their pre-exposure values. However, when comparing the DPOAE amplitudes pre- and post-traumatic exposure for the control group, statistically significant reductions were found at all frequencies tested. In particular, at 1.75-, 2.1-, and 2.8 kHz, DPOAE amplitudes failed to increase despite an increase in primary tone levels over a 40 dB range. The analysis of surface preparations of the organ of Corti revealed that the pattern of OHC damage was different between the two groups. There were two distinct peaks in the cochleograms (graphs of the % of hair cell loss vs. the distance from the round window) of the sound conditioned group corresponding to two distinct regions of OHC loss along the cochlear partition. The underlying cause for this modified pattern of cochlear damage was not given. Interestingly though, the sound conditioned group suffered 50% less OHC loss than the control group. Thus, the results of this study demonstrated that sound conditioning prior to exposure to a traumatic auditory stimulus maintained the amplitude of DPOAEs over a wide frequency range, reduced the degree of OHC loss, and caused an altered pattern of OHC damage. The authors suggested that the intrinsic properties of the OHCs and/or organ of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Corti may have been altered by the low-level, long-term exposure, thus rendering the cochlea less susceptible to the damaging effects of the traumatic exposure.

Despite the methodological differences within the studies mentioned above, the overall findings were consistent. That is, prior exposure to low-to-moderate level conditioning noise resulted in less PTS when compared to that found in control (traumatic exposure only) subjects. However, evidence has also been reported which contradicts the protective role of the conditioning noise exposure (Subramaniam et al., 1992, 1993b; Fowler et al., 1995).

Subramaniam et al. (1992) were interested in determining if the basal region of the cochlea could be made more resistant to noise-induced hearing loss by prior exposure to high frequency, moderate-level noise. They examined the role of a high frequency, moderate-level conditioning exposure in providing protection against hearing loss from subsequent exposure to the same noise spectrum presented at a higher level. Chinchillas that were deafened in one ear were then exposed to an 85 dB SPL octave band noise centered at 4 kHz for 6 hours per day (6 hours "on"/18 hours "off") for 10 consecutive days. The 4 kHz octave band noise produced a reduction in threshold shift from day 1 to day 10 (toughening) which supports the results reported in an earlier study (Subramaniam et al., 1991b). These conditioned animals were then assigned to

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

two groups depending upon the length of time allowed for recovery from the moderate-level exposure. One group was allowed to recover for 5 days and the other for only 18 hours before being exposed to the traumatic exposure (100 dB SPL octave band noise centered at 4 kHz for 48 hours). Results showed that the group of conditioned animals that recovered for only 18 hours had 10-15 dB of residual hearing loss at test frequencies 8- and 16 kHz. However, the group given 5 days to recover demonstrated no residual hearing loss at any of the test frequencies (0.5 - 16 kHz in one octave steps and the mid-octave frequency of 5.6 kHz). Control animals were also deafened in one ear, but were exposed only to the 100 dB SPL noise for 48 hours. Hearing thresholds determined using evoked potential recordings were measured in all three groups of animals immediately upon removal from the traumatic noise and then 24 hours, 5 days, and 4 weeks post-exposure. In addition, inner and outer hair cell damage was assessed histologically to determine the presence or absence of hair cells along the length of the cochlea. The results of the initial measurement (taken immediately upon removal from the traumatic noise) showed that the 5 day recovery group had the least amount of threshold shift of the three groups tested at the center frequency of the noise and one half octave above it (4- and 5.6 kHz, respectively). By 24 hours post-exposure, the threshold shifts measured in all three groups were approximately equal. Interestingly,

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

measurements taken 4 weeks post-exposure revealed that the 18 hour recovery group incurred considerably less PTS and total hair cell loss than the other two groups. The group of animals allowed 5 days to recover from the conditioning noise, however, demonstrated greater amount of PTS than the other groups, although hair cell loss for this group was comparable to that of the control group. The authors attributed the lack of protection found in the 5 day recovery group to the transitory nature of the protective changes that may have occurred within the auditory system during conditioning, but then dissipated over the course of the 5 day recovery period. They concluded that the differences in their results, when compared to results reported by Campo et al. (1991), reflected basic biological differences between the base and the apex of the cochlea.

In an attempt to determine the generality of the conditioning effect (i.e., does conditioning protect the entire cochlea or is the effect restricted to the region of the exposure frequency), Subramaniam et al. (1993b) studied whether conditioning with low frequency noise protected the auditory system from subsequent high frequency exposures. Chinchillas were first deafened in one ear and then conditioned using a 95 dB SPL octave band noise centered at 0.5 kHz for 6 hours a day (6 hours "on"/18 hours "off") for 10 consecutive days. The animals were then allowed to recover for 5 days in a quiet environment. The animals were then exposed to a high frequency traumatizing noise

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(100 dB SPL octave band noise centered at 4 kHz for 48 hours). Control animals were also deafened in one ear, but exposed only to the higher level noise. Hearing thresholds were measured using evoked potential recordings in all three groups of animals immediately upon removal from the traumatic noise and then 24 hours, 5 days, and 4 weeks post-exposure. In addition, inner and outer hair cell populations were assessed to determine hair cell damage along the length of the cochlear partition. Thresholds were beyond the limits of the equipment in many control and conditioned animals tested immediately after the intense exposure, but recovered considerably over the next 24 hours. The magnitude of PTS observed in the conditioned group was significantly higher than that of the control group at test frequencies greater than or equal to 4 kHz. The difference in PTS was about 10 dB at 4 kHz and 25 dB at frequencies from 5.6- to 16 kHz. Group differences were also confirmed by the histological results, with the conditioned group incurring greater OHC loss than the control group. The results showed that low frequency conditioning did not offer protection against subsequent exposures to high frequency noise. Instead, prior exposure to low frequency noise rendered the auditory system more susceptible.

Fowler et al. (1995) found that the conditioning exposures used in their experimental paradigm acted to enhance, rather than diminish, the damaging effects of the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

traumatic exposure when using the CBA/Ca mouse as the experimental animal. The authors stated that they were interested in investigating the protective role of the conditioning exposure in the mouse because its pattern of hearing sensitivity was markedly different than all of the animal models studied thus far (i.e., guinea pigs, rabbits, chinchillas, gerbils, and humans). Studies by Henry (1983) and Li and Borg (1991) determined that mice have their greatest sensitivity between 6.3- and 24 kHz, whereas the audibility curves of the other species mentioned show greatest sensitivity between 0.5- and 16 kHz. The authors observed that the majority of previous studies demonstrating the protective role of prior sound conditioning used low-to-moderate level noise or pure tones in the lower end of the audibility curve of the species tested. In this study, a narrowband noise centered at 4.5 kHz was used for both the conditioning and the traumatic noise exposures. This exposure was expected to produce the greatest threshold shift at approximately 6 kHz (½ octave above the center frequency of the noise) which is near the lower end of the mouse audibility curve, but still within a relatively sensitive region. Groups of animals were exposed to different conditioning exposures, presented continuously or on an interrupted schedule (6 hr "on"/18 hr "off"), for either 10 or 24 consecutive days. The various levels of noise used for the conditioning exposures were chosen because they induced either no, minimal, or moderate

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

threshold shifts as measured by reductions in the auditory brainstem response thresholds at 4.0-, 6.3-, 8.0-, 10.0-, 12.5-, and 16.0 kHz. Following these measurements, the animals were allowed 6 to 8 hours to recover from the effects of the anesthesia before being exposed to the traumatic noise. The traumatic noise was presented at several levels (107, 110, or 117 dB SPL) for 24 hours to induce temporary or permanent hearing loss of graded severity. Control groups were exposed only to one of the high-level exposures. Auditory brainstem response thresholds were then measured approximately 12 hours, 1 week, and 4 weeks post-traumatic exposure. Results showed that protection against the damaging effects of a traumatic noise exposure was not found, no matter which combination of sound conditioning paradigm (i.e., continuous or interrupted) and level of traumatic noise was used. In fact, in most cases, there was a tendency for the conditioned animals to demonstrate greater reductions in threshold after the traumatic exposure than the control group. Thus, these results contradicted the previous reports that showed that sound conditioning was an effective means of providing up to 30 dB of protection against subsequent noise trauma. Fowler et al. (1995) attributed their negative findings to peculiarities in the response of the mouse auditory system to noise trauma.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**2.3 Mechanisms Responsible for Protection**

Although many studies have demonstrated that prior sound conditioning affords protection against subsequent noise exposures, the physiological mechanism(s) responsible for these results is still unknown. A number of possibilities have been suggested to account for the protective function of the conditioning noise exposure. These include: (1) improvement in the attenuation provided by an increased strength of the middle ear muscles (MEMs) in conjunction with the acoustic reflex; (2) changes in efferent activity; and (3) changes in cochlear physiology (in particular, OHC physiology).

The role of the MEMs as a potential mechanism for providing protection against noise exposure in animals that have been previously conditioned has been evaluated in chinchillas (Henderson et al., 1994), gerbils (Ryan et al., 1994), and guinea pigs (Dagli and Canlon, 1995). The underlying basis of this proposed mechanism is the idea that the MEMs, and hence the acoustic reflex, become stronger over the course of the moderate-level conditioning exposure. This could potentially lead to an improvement in the amount of attenuation generated by the acoustic reflex in response to subsequent high-level exposures. The results of the studies by Henderson et al. (1994) and Ryan et al. (1994) demonstrated that groups of sound conditioned animals, both with and without sectioned MEMs, developed significantly less PTS than groups of control animals that

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

had not been conditioned. However, no difference was found in the amount of PTS between the groups of animals with sectioned vs. intact MEMs. Dagli and Canlon (1995) compared the amount of decrease, duration of the loss, and the rate of recovery of DPOAE amplitudes in response to a TTS-producing exposure in sound conditioned guinea pigs with either paralyzed or intact MEMs. Significant differences were not found in the DPOAE measurements between the two groups of guinea pigs. Thus, the results of the studies mentioned above do not support a role for the MEMs in providing protection against traumatizing noise.

A number of studies have suggested that activation of the medial cochlear efferent system can protect the inner ear from acoustic injury (Cody and Johnstone, 1982; Puel et al., 1988b; Rajan, 1992). However, to date, there is no definitive evidence in support of a protective role of the medial cochlear efferent system during noise exposure. Most of the studies that have addressed this issue have used very short duration (< 10-15 min), high intensity (> 100 dB) pure-tone exposures. One set of studies using this type of exposure for guinea pigs indicated that the effects of noise were reduced by activation of the medial cochlear efferents by either electrical or contralateral stimulation (Rajan and Johnstone, 1983; Rajan, 1992). However, Liberman (1992) was unable to replicate these results in

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

cat and suggested that the efferents did not play a role in protecting the auditory system.

In a recent study, Rajan (1996) examined whether the protective role of sound conditioning was mediated by the medial cochlear efferent system. An experimental group of guinea pigs was conditioned with a 97 dB SPL 10 kHz pure-tone for 1 minute. After a 40 minute rest, the animals were then exposed to a high-level exposure (103 dB SPL 10 kHz pure-tone for 1 minute). A control group of animals was exposed only to the high-level tone. Significantly less threshold shifts were recorded over the most affected frequency range (10-20 kHz) after the high-level exposure in the conditioned group of animals as compared to the shifts recorded in the control group. These results are in accordance with the earlier findings of Canlon et al. (1988) and Campo et al. (1991). Two additional groups were then tested to determine the role of the medial cochlear efferents in this protection phenomenon. In the first group, an intraperitoneal injection of strychnine (10 mg/kg body weight) was given to the animals approximately 15 minutes prior to sound conditioning, while in the second group, strychnine was administered approximately 15 minutes after the conditioning exposure. Strychnine is a known blocker of the medial cochlear efferent system (Kujawa et al., 1993, 1994; Erostegui et al., 1994). When the thresholds of these two strychnine-treated groups were measured after the high-level exposure and compared with

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the results of the previous two groups described above, it was found that the strychnine treatment (no matter when it was administered) did not affect the ability of the conditioning exposure to reduce the damage caused by the subsequent high-level tone. The threshold shifts in these two groups were not significantly different from the shifts recorded in the group that was only exposed to the conditioning exposure and not treated with strychnine. However, the losses were significantly less in the conditioned groups, no matter how they were treated, than the losses measured in the control group. Thus, these results suggest that the medial cochlear efferents do not play a role in mediating the protection from acoustic trauma induced by prior sound conditioning. These results were supported by the findings of Canlon et al. (1992) showing no morphological changes in the efferent synapses under the OHCs after sound conditioning. Rajan (1996), however, did not totally exclude a role for the efferents in this type of protection. He concluded that on the basis of the evidence found, it can only be stated that the medial cochlear efferents are not involved. He did not discount the possibility that other subsystems of the cochlear efferents might be responsible for the protection afforded by the sound conditioning.

Canlon et al. (1992, 1993) hypothesized that changes in cochlear physiology, particularly changes occurring within the OHCs during sound conditioning, may be

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

responsible for the protective effect of the conditioning noise. The results of electron microscopy studies revealed an increase in the intracellular membrane components (e.g., vesicles, coated vesicles, tubulovesicular cisternae) in the infranuclear region of the OHCs in animals that had been exposed to a low-level conditioning noise (1 kHz, 81 dB SPL for 24 days). Interestingly, although these changes were found, exposure to this low-level, long-term acoustic stimulus did not cause changes in auditory sensitivity. The increase in intracellular membrane components indicated that there is a capacity for this region of the OHC (presynaptic area opposing the afferent synapse of the OHC) to undergo increased membrane recycling in response to a long-term exposure. This "upregulation" of membrane recycling may act to increase the neurotransmitter pool of the OHCs (by improving synthesis and uptake mechanisms) which in turn, may act to enhance synaptic efficiency. Canlon et al. (1992, 1993) concluded that this stimulus-related improvement in synaptic efficiency (as suggested by the increase in vesicle content in the presynaptic afferent region of OHCs) might allow the system to better endure the damaging effects of the subsequent exposure.

It has also been hypothesized that sound conditioning increases the amount of protective cellular proteins expressed within the cochlea (in particular, the OHCs), thus providing protection against the damaging effects of subsequent noise trauma. Heat shock proteins (HSPs) are a

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

group of proteins that are expressed in almost all cells in almost all species in response to a variety of stresses (e.g. heat shock, viruses, ischemia, drugs, oxygen radicals, nutrient deprivation, etc.). HSPs are believed to be involved in the acquired tolerance to stress (meaning that a prior stress-inducing exposure decreases the pathological effect of a second, more severe stress-inducing exposure; Lindquist and Craig, 1988; Welch, 1992). Barbe et al. (1988) reported that hyperthermia caused increases in the level of expression of HSPs in rat retinal cells which acted to protect the retina from subsequent light damage. Hutter et al. (1994) determined that hyperthermic stress protected against infarct after periods of ischemia. Several investigators have demonstrated the expression of HSPs in both the guinea pig and rat cochlea. In guinea pigs, expression was found in the cochleae of normal, unstressed animals (Neely et al., 1991); however, the level of expression was increased under conditions of hyperthermic stress (Thompson and Neely, 1992). In rats, no expression of HSPs was found in cochlea taken from unstressed animals; however, expression was induced by heat shock (Dechesne et al., 1992) and transient hypoxia (Myers et al., 1992). Recently, an upregulation in the expression of certain HSPs has been shown in rat OHCs in response to acoustic overstimulation (Lim et al., 1993, 1994, 1996; Ditto et al., 1994; Altschuler et al., 1996). It is uncertain whether this noise-induced elevation in the level

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

of expression of these proteins is responsible for providing protection against later exposures. However, the fact that HSPs serve a protective function in cells within other systems lends support to the notion that HSPs could also be involved in protecting the auditory system from noise-induced trauma.

Calcium is known to play an important role in the regulation of a variety of physiological processes. Canlon and Fransson (1994) were interested in determining the effect of sound conditioning on calcium homeostasis in the guinea pig cochlea. Calbindin D-28 kDa is a calcium-binding protein that is abundant in the inner ear and is thought to play an important role in auditory transduction and hair cell homeostasis (Oberholtzer et al., 1988; Christakos et al., 1989). Canlon and Fransson (1994) showed that in normal guinea pig cochleae, calbindin D-28 kDa is localized to the cytoplasm of both IHCs and OHCs, with high levels of immunoreactivity in the cuticular plate of the cells and low levels in cell nuclei. Immediately after exposure to a low-level conditioning tone (1 kHz, 81 dB SPL, 24 days), a dramatic decrease in the immunoreactivity of the calcium-binding protein was found in both types of cells. This decrease was long-term in that it required approximately 30 days of rest from the conditioning exposure until control levels of immunoreactivity were again attained. This result suggested that the effects of sound conditioning were

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

long-lasting. Interestingly, the protective effect of the conditioning exposure was still evident in animals maintained in quiet environments for one month prior to the subsequent traumatic exposure. The authors proposed that the decrease of calbindin D-28 kDa immunoreactivity may be caused by the inhibition of calcium movement into the hair cells during the prolonged low-level acoustic stimulation. Decreased calcium influx could act to protect the cells by rendering them less excitable. The authors claim that the physiological significance of these results remains to be determined.

**2.4 Distortion-product otoacoustic emissions (DPOAEs)**

When the ear is stimulated by two continuous pure tones, known as primary tones ($f_1$ and $f_2$; $f_1<f_2$), the cochlea generates intermodulation distortion products that can be measured in the external auditory canal. These distortion products (e.g. $f_2-f_1$, $2f_1-f_2$, $3f_1-2f_2$, etc.), referred to as distortion-product otoacoustic emissions (DPOAEs), are believed to reflect the mechanical properties of the cochlea, particularly as related to the status of outer hair cell (OHC) function (Mountain, 1980; Siegel and Kim, 1982; Siegel et al., 1982). DPOAEs are generated via nonlinear cochlear processes associated with the region along the basilar membrane that corresponds to the region of maximum interaction of the primary tones. This region is believed to be near, or at, the $f_2$ place on the basilar membrane (Brown et al., 1992; Allen and Fahey, 1993; Puel

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

et al., 1995). From their generation site, the distortion products are propagated by fluid dynamics: (1) apically to the place tuned to the distortion product frequency, giving rise to audible combination tones (Smoorenburg, 1972) and eliciting tuned VIIIth nerve responses (Kim, 1980); and (2) basally towards the stapes and through the middle ear, giving rise to measurable acoustic signals (DPOAEs) within the external canal (Kemp, 1979). A small amount of acoustic energy measured within the external canal may also come from the more apical location on the basilar membrane where the distortion product frequency reaches a maximum (Wilson, 1980).

The amplitude growth of the cubic ($2f_1$-$f_2$) DPOAE with increasing primary level has been shown to be nonmonotonic (Brown, 1987). This finding is analogous to the psychoacoustic observations of Smoorenburg (1972). The nonmonotonic nature of the amplitude growth function suggests that different mechanisms are acting in the generation of DPOAEs elicited by either low-to-moderate vs. high-level (>60 dB) primary tones. The low intensity portion of the amplitude growth function is linear and DPOAE amplitude increases with stimulus level up to approximately 60 dB. DPOAEs elicited by low-to-moderate level primaries are physiologically vulnerable to the same factors (e.g., noise exposure and ototoxicity) that normally damage or destroy OHC function (Kim, 1980; Zurek et al., 1982; Brown et al., 1989; Mills et al., 1993;

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Subramaniam et al., 1994a,b). These observations suggest low-level distortion product generation is associated with the active, nonlinear processes of the OHCs. Above 60 dB, the growth function either saturates, rolls over, or the DPOAE amplitude increases more rapidly with stimulus level than at lower primary levels (slope increases). The generation of DPOAEs elicited by high-level primaries usually is attributed to the passive mechanical properties of the cochlea since these emissions are relatively invulnerable to cochlear insult (Zurek et al., 1982) and can even be measured in the ear of a dead animal (Schmiedt and Adams, 1981; Pers. observ.). In some animals, there is a "notch" in the I/O functions that occurs when the level of the primary tones is around 60-65 dB. Brown (1987) suggests that the occurrence of this notch may be due to interaction between out-of-phase components of low- vs. high-distortion generation.

**2.5 The Equal Energy Hypothesis**

The Equal Energy Hypothesis (EEH), as proposed by Eldred et al. (1955), represents an attempt to formulate a unified and relatively simple strategy to estimate the auditory hazard associated with a wide range of noise exposure conditions. The EEH assumes that the cumulative damage to the auditory system is a function of the total acoustic energy received, regardless of the distribution of energy over time. Simply stated, noise exposures of equal energy imply equal risk for noise-induced hearing loss. It

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

follows that the total acoustic energy of an exposure is given by the product of the intensity of the noise and the duration of the exposure. The EEH describes a reciprocal trading relationship between the intensity and the duration of the noise exposure. Thus, for the total acoustic energy (and therefore, the amount of hearing loss) to remain constant, the exposure intensity must be doubled (increased in level by 3 dB) each time the exposure duration is halved and vice versa. The inherent simplicity of the EEH, and the ease with which its basic concepts can be incorporated into instrumentation to produce a single number "index" of the hazards of any noise environment, established it as one of the first damage-risk criterion measures in the United States in 1956 (U.S. Air Force Regulation 160-3). The EEH damage-risk estimation scheme was later formally adopted by the International Organization for Standardization (1981).

Several demographic studies have led to the promotion of the EEH as a model on which to base noise standards and damage-risk criteria. Burns and Robinson (1970) formalized the EEH, providing the most convincing demographic evidence of its validity in the case of permanent noise-induced hearing loss from industrial, steady-state noise. These results were supported by Passchier-Vermeer (1974); however they fit their data to an alternative mathematical formulation of the EEH which they had developed. Atherley and Martin (Atherley and Martin, 1971; Atherley, 1973; Martin, 1976) extended the work of Burns and Robinson

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(1970) in order to apply the EEH to impulse and impact noise exposures. Their data, acquired from a group of employees in the drop-forge industry, was also in accordance with the EEH, at least up to peak levels of 150 dB SPL (Martin, 1976). Other investigators have also reported that the hazard from impulse and impact noise may be predicted by the EEH (Guberan et al., 1971; Kuzniarz et al., 1976).

However, the results of several other demographic studies investigating the effect of impulse noise on permanent threshold shift are in conflict with the predictions derived from the EEH (Sulkowski et al., 1980, 1983; Voigt et al., 1980; Taylor et al., 1984). Sulkowski et al. (1980, 1983) found that workers exposed to impulse noise demonstrated greater hearing loss than workers exposed to industrial steady-state noise of equal acoustic energy. Voigt et al. (1980), reported that for equal average levels, there was an increased risk for hearing loss in construction workers exposed to widely fluctuating noise levels as opposed to those exposed to more stable noise levels. Thus, because of this negative evidence, controversy still remains concerning the validity and general applicability of the EEH as a model for predicting hearing loss. In addition, many have reported that the data collected in these large scale demographic studies was fraught with extreme intersubject variability, making it such that a variety of analytic formulations could be used

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

to adequately describe the data (Taylor and Pelmear, 1976; Roberto et al., 1985; Henderson et al., 1991).

A number of studies using laboratory animals as subjects also do not provide conclusive evidence for the overall applicability of the EEH, especially as it applies in cases of impact and impulse noise exposures (Roberto et al., 1985; Henderson et al., 1991). For instance, Ward et al. (1981) subjected different groups of chinchillas to a series of continuous noise exposures of approximately equal energy (150 days at 82 dB SPL; 15 days at 92 dB SPL; 1.5 days at 102 dB SPL; 0.15 days at 112 dB SPL; 0.015 days at 120 dB SPL). They reported that for all exposures up to and including 112 dB SPL, the same amount of PTS and OHC loss was found, thus confirming the validity of the EEH for assessing the hazard associated with single, continuous exposures at moderate intensities. However, the 120 dB SPL exposure yielded a much larger hearing and OHC loss than was predicted by the EEH, given an exposure of equal acoustic energy. The authors suggested that a critical exposure level may exist that, when exceeded, the rules for time-intensity trading would not hold.

A critical exposure level was also found in chinchillas after exposure to impact noises of various intensities (107-125 dB peak SPL) and durations (120-1.87 hours) presented at a fixed rate of four impacts per second (Roberto et al., 1985). Again, the exposure conditions were balanced to produce exposures of approximately equal

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

energy. The damaging effects of the exposures were assessed by measuring auditory evoked response thresholds and the amount of hair cell loss of the four different exposure groups. Results showed that the amount of PTS and the percent hair cell loss were approximately equal following the exposures to the 107-, 113-, and 119 dB peak SPL impact noises, but significantly higher for the 125 dB peak SPL exposure. Thus, according to these results, the EEH was valid below some critical exposure level. This provided support for the findings of Ward et al. (1981), and suggested that above some critical combination of level and duration for impact noise exposures, auditory hazard would be substantially greater than would be predicted from equivalent energy considerations.

Henderson et al. (1991) extended the work of Roberto et al. (1985) to include higher peak intensities and additional repetition rates. In the first part of their experiment, six exposure levels (107-, 113-, 119-, 125-, 131-, and 137 dB peak SPL) and three repetition rates (4/second, 1/second, and 1/4 seconds) were used. The durations of the exposures were varied such that the total energy of each exposure condition was approximately the same. In the second part of this experiment, the duration of the exposure was held constant, but the exposure level and the repetition rate were traded to keep the total energy constant. Hearing thresholds were estimated by recording the auditory evoked potentials from an electrode

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

implanted in the inferior colliculus and histological analysis was performed to determine the amount of hair cell loss. The overall results of this experiment indicated that the auditory hazard acquired from exposure to impact noise was not solely dependent upon the total amount of energy within the exposure (as implied by the EEH), but on the interaction of several factors such as the peak level and duration of the exposure, the repetition rate of the impacts, and the susceptibility of the animal. Although the amount of PTS and hair cell loss were similar for the lower peak exposure levels, both measures were significantly higher for the exposures of higher peak levels. These results are consistent with the hypothesis that, for impact noise, there is some critical level above which the rules for the EEH do not hold and the magnitude of hearing loss is much greater than would be predicted (Roberto et al., 1985). Henderson et al. (1991) estimated that for chinchillas, this critical level was between 119 and 125 dB peak SPL, depending upon the repetition rate of the impacts within the exposure.

Industrial work environments usually consist of combinations of continuous noise and moderate levels of impact noise. Ahroon et al. (1993) evaluated the applicability of the EEH to such complex noise environments, since a number of investigators have reported that simultaneous exposure to different classes of noise may exacerbate the effects of a given noise exposure

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(Hamernik et al., 1974; Hunt et al., 1976). Groups of chinchillas were exposed for 5 days to either octave bands of noise, impact noise, or a combination of the two types of noise exposures. Noise-induced trauma was quantified using auditory evoked potential threshold measurements and histological analysis to determine hair cell loss. The results clearly demonstrated that there were exposure conditions which produced levels of trauma that would not be anticipated on the basis of the EEH. When the impact noises were presented alone, the three different 5-day exposures, all with equal acoustic energy, induced equivalent audiometric and histologic effects. However, when these same exposures were combined with continuous noise, equivalent exposure energies did not yield equivalent levels of trauma. Ahroon et al. (1993) pointed out that according to their results, differences in the amount of hearing loss from equal energy exposures are not only dependent upon the total amount of exposure energy, but also on such factors as the repetition rate of the impact noise and the frequency spectrum of the superimposed continuous octave band noise.

In spite of the negative findings summarized above, the EEH does appear to have some predictive value for intensities (and other exposure conditions) observed in most industrial environments (Atherley and Martin, 1971). The continuous and interrupted conditioning exposures used in the present study seem to fall within the range of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

exposure conditions for which the EEH is generally applicable. These particular exposures were chosen for this reason and also because of their similarities to exposures used in similar types of sound conditioning experiments.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CHAPTER 3

# METHODS

## 3.1 Subjects

Experiments were performed on 84 pigmented guinea pigs (*Cavia cobaya*) of either sex weighing between 500 and 850 grams. The guinea pigs were supplied by a licensed breeder (Parker's Cavies, Slidell, LA 70458). During periods of noise exposure, the animals were housed in a small sound attenuating booth (See Section 3.2.1 for description). Unexposed animals, along with animals recovering from the noise exposure, were housed and cared for by Louisiana State University Medical Center's Animal Care facility, approved and certified by the American Association of Laboratory Animal Science.

Only animals with a normal Preyer reflex and no obvious outer or middle ear pathology were included in the study. All animals used in this study were treated in accordance with federal, state, and institutional guidelines and the NIH Guide for the Care and Use of Laboratory Animals (National Institutes of Health, 1985). The care and use of the animals were approved by the Medical Center's Institutional Animal Care and Use Committee.

## 3.2 Noise Generation and Exposure Methods

### 3.2.1 Noise exposure facility

During periods of noise exposure, unanesthetized guinea pigs were housed in groups of 10 or less in a small



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

sound-attenuated booth (approx. interior dimensions 76 × 60 × 40 cm; Industrial Acoustics Company, Inc., Serial #101655) contained within a larger sound-attenuated booth (Industrial Acoustics Company, Inc., Serial #106138). The walls of the smaller booth were lined with hard, reflective surfaces to produce uniform sound levels throughout the chamber. The speaker was mounted on a wooden surface which covered the booth ceiling. The speaker was approximately 40 cm above the level of the guinea pigs' ears. A small light was also mounted on the wooden surface. The light was controlled by a timer which allowed for 12 hours of illumination and 12 hours of darkness. This sequence of light and dark periods provided the animals with a simulated diurnal cycle. Small holes were drilled into the wood (in irregular patterns) beneath the intake and exhaust vents to allow for proper air exchange within the booth. A small exhaust fan was mounted on the side of the booth for additional ventilation. The floor of the booth was lined with a metal pan filled with animal bedding (Sani-Chips).

### 3.2.2 Noise generation and calibration procedures

Both the moderate-level conditioning noise and the traumatizing noise were generated by a WG2 Waveform Generator (Tucker-Davis Technologies) which was set in the "Uniform" mode. This signal was bandpass filtered using a Brickwall Filter (Wavetek/Rockland Model 753A) with a low frequency cutoff at 1.0 kHz, a high frequency cutoff at 2.0 kHz, and a roll-off of 115 dB/octave. The level of the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

filtered noise was controlled by a PA4 Programmable Attenuator (Tucker-Davis Technologies). Additional power was gained using a power amplifier (McIntosh MC2100) producing the final signal that was delivered to the speaker (Realistic 40-1286C; 8Ω, 30 watts).

The spectrum of the noise used in this study was an octave band noise with the low- and high-cutoff frequencies at 1.0 and 2.0 kHz, respectively. The continuous and interrupted schedules of the moderate-level conditioning noise had equal acoustic energy as defined by the EEH (Eldred et al., 1955). As mentioned earlier, the EEH implies that for every doubling of exposure duration, the intensity of the noise must be decreased by 3 dB for the total acoustic energy to remain constant. In this study, the continuous conditioning noise was presented at a level of 89 dB SPL (A-scale) for 24 hours per day for 11 days, while the interrupted conditioning noise was presented at a level of 95 dB SPL (A-scale) for 6 hours per day (6 hours "on"/18 hours "off") for 11 days. The high-level traumatizing noise was presented continuously for 3 days at 105 dB SPL (A-scale). These levels were chosen because they approximated the levels of conditioning and traumatizing noises used in previous studies concerned with this type of protection phenomenon (Canlon et al., 1988; Campo et al., 1991).

Noise levels were monitored daily using a ½ inch condenser microphone (Brüel & Kjaer Type 4133) and

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

preamplifier combination that were connected to a measuring amplifier (Brüel & Kjaer Type 2610). This system was calibrated with a sound level calibrator (Brüel & Kjaer Type 4230) which produces a nominal sound pressure of 94 dB ± 0.3 dB (re: 20 μPa). The microphone was positioned so that it was approximately at the level of the guinea pigs' ears and was placed at various positions around the booth to ensure that the noise was equally distributed throughout the booth. Noise levels were found to vary ± 2 dB depending upon microphone position. The background level inside the booth with the noise off, doors closed, and animals present was approximately 40 dB SPL (A-scale). The voltage across the speaker was also checked daily using a digital voltmeter (Wavetek Corporation BI-DM15XL). The voltages corresponding to the levels of noise used in this study, i.e., 89, 95, and 105 dB SPL, were approximately 0.45, 0.90, and 2.9 volts (rms). The linearity of the speaker (and noise generation system) was verified by converting the ratios of these voltages to dB to make certain that this value coincided with the amount of change (in dB) of the attenuator setting.

The spectrum of the noise was obtained by connecting the AC output of the measuring amplifier (Brüel & Kjaer Type 2610) to the input of a signal analyzer (Hewlett-Packard 3561A). The spectrum of the noise is shown in Figure 1 for each exposure level.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

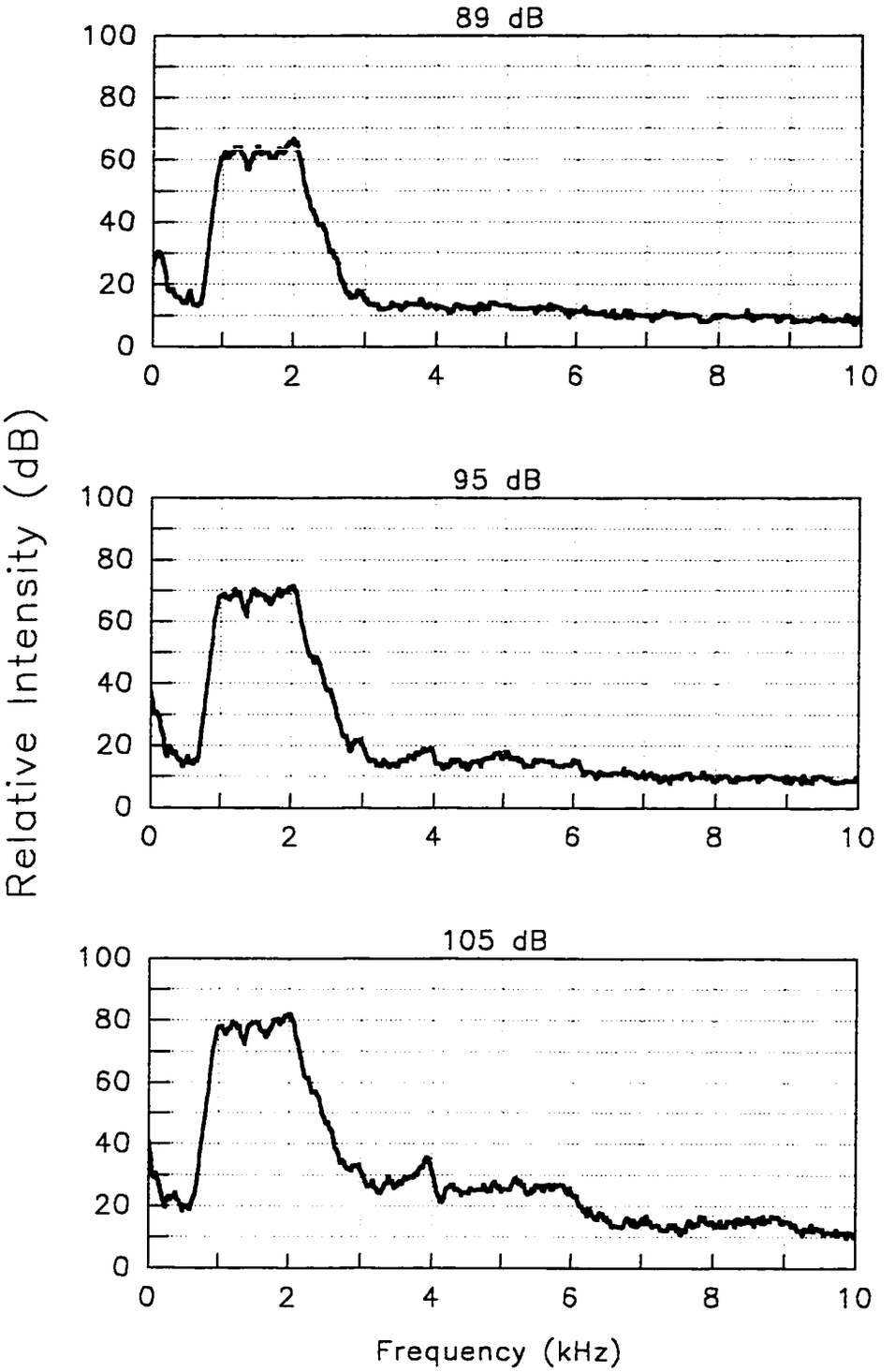


**Figure 1.** Spectral characteristics of the continuous conditioning noise (89 dB SPL; top), the interrupted conditioning noise (95 dB SPL; middle), and the traumatizing noise (105 dB SPL; bottom) exposures. The graphs represent the relative intensity of the noise exposures (dB) plotted as a function of frequency (kHz).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

### 3.3 General surgical methods

Immediately prior to testing, the animals were anesthetized by administering a dose of urethane (ethyl carbamate, Sigma; 1.5 g/kg, i.p.), tracheotomized, and allowed to breathe unassisted. Supplementary doses of anesthetic (urethane, 1.5 g/kg) were given if necessary to maintain an adequate depth of anesthesia (as indicated by a lack of a withdrawal response to deep pressure and pain applied to the animal's paw). Electrocardiogram and rectal temperature were monitored throughout each experiment and temperature was maintained at 38 ± 1°C using a heating pad.

The surgical procedures used were similar to those described by Kujawa et al. (1992, 1993). Briefly, cartilaginous ear canals were exposed and partially removed to allow for proper placement of ear bars used to secure the animal in a modified Narishige stereotaxic headholder. This procedure also ensured optimal coupling of the sound delivery and response retrieval system to the test ear. Using a ventrolateral approach, the ipsilateral (right) auditory bulla was exposed and opened to gain access to the tendons of the middle ear muscles. These tendons were sectioned in all animals to prevent the involvement of middle ear muscle contraction on the DPOAE measurements.

The surgical procedures required approximately 1½ hours to complete. All experiments were acute. At the end of the experiment, the head was removed from the rest of the body using a small guillotine to terminate the animal.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

This procedure is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association (1993).

### 3.4 DPOAE generation and calibration procedures

Cubic ($2f_1$-$f_2$) DPOAEs were elicited by the presentation of equilevel ($L_1$=$L_2$) primary tones ($f_1$ and $f_2$) at various frequencies which yielded a $f_2/f_1$ ratio of 1.2. The primaries were generated under computer control using Tucker-Davis System 2 audio processing equipment. More specifically, the computer generated primaries were sent to two separate channels of a DA1 Digital-to-Analog Converter and attenuated to desired levels using PA4 Programmable Attenuators. The attenuated analog signals were then sent to two separate channels of an anti-aliasing low-pass filter with a 20 kHz cutoff frequency (FT5) and then to the HB5 Headphone Buffer before being sent to separate speakers (Etymotic Research, ER-2) housed within an acoustic probe assembly. The acoustic probe assembly was tightly coupled to the right ear of each animal. DPOAEs were then detected by a sensitive microphone (Etymotic Research, ER-10) also housed within the probe assembly and amplified using a microphone preamplifier (Etymotic Research, ER-1072). A dynamic signal analyzer (Hewlett-Packard, 3561A) was used to average the DPOAE responses for FFT analysis and spectral display (25 rms averages; center frequency = DPOAE frequency; span = 1 kHz; bandwidth = 3.75 Hz).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Calibration of the primary tones was performed at the outset of the study and then twice a week thereafter. This was accomplished by coupling the acoustic probe assembly to a ¼ inch condenser microphone (Brüel & Kjaer Type 4135) and then cross-checking the output of the speakers using (1) the ER-10 probe microphone and (2) the B&K condenser microphone. The signal from the probe microphone and preamplifier (ER-10 and ER-1072) was sent to the signal analyzer and the level of each of the primary tones was obtained from the spectral display (center frequency = primary tone frequency; span = 1 kHz; bandwidth = 3.75 Hz). For this system, the conversion of dBV to dB SPL was obtained by adding 120 to the dBV value at the peak of the corresponding primary frequency. The signal transduced by the condenser microphone and preamplifier was sent to the measuring amplifier (Brüel & Kjaer Type 2610) and the level of the primary tones was indicated by the deflection of the needle on the meter scale (measured in dB SPL). The equivalence of the primary levels using both measurement systems was verified at each calibration session.

### 3.5 DPOAE input-output measurements

Cubic ($2f_1$-$f_2$) DPOAEs were measured for several combinations of $f_1$ and $f_2$ (See Table 1). For the proposed experiments, the $f_2/f_1$ ratio was held constant at 1.2, which is within the range describing the optimal frequency separation of $f_1$ and $f_2$ for the guinea pig (1.2-1.3; Brown, 1987; Brown and Gaskill, 1990). This ratio has been used

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 1.** Primary tones and corresponding DPOAEs (measured in Hz)

| $f_1$ | $f_2$ | $2f_1-f_2$ |
|---|---|---|
| 589 | 707 | 471 |
| 833 | 1000 | 667 |
| 1178 | 1414 | 943 |
| 1667 | 2000 | 1333 |
| 2357 | 2828 | 1886 |
| 3333 | 4000 | 2667 |
| 4713 | 5656 | 3770 |
| 6667 | 8000 | 5334 |
| 9427 | 11312 | 7542 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

previously in our laboratory (Kujawa et al., 1992, 1993) and has been adopted as a laboratory standard for purposes of comparing old and new DPOAE data. In addition, because the place of the DPOAEs is believed to be near, or at, the $f_2$ place on the cochlear partition (Matthews and Molnar, 1986; Brown et al., 1992; Allen and Fahey, 1993; Puel et al., 1995), all data were expressed as a function of $f_2$ rather than the actual frequency of the DPOAE. These particular values of $f_2$ were chosen for study because their corresponding frequencies map out (in half octave steps) the frequency spectrum of the noise band used to expose the animals and the region of possible OHC loss along the cochlear partition.

DPOAE responses were elicited with equilevel primaries ($L_1=L_2$). The primary tones were presented in descending order, starting at a level of 70 dB SPL and decreasing in 5 dB steps to 20 dB SPL. The amplitudes of the DPOAEs, defined as the spectral peak corresponding to the $2f_1-f_2$ frequency (as viewed on the signal analyzer), were recorded manually in dBV from the FFT spectra (25 averages) and later converted to dB SPL (re: 20 $\mu$Pa). Plots of primary level vs. DPOAE amplitude (amplitude growth functions) were generated.

### 3.6 Experimental design and noise exposure protocols

The experiment was designed to examine the effects of a high-level (traumatizing) noise exposure on DPOAE amplitude growth functions in animals that have been

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

conditioned with moderate-level continuous or interrupted noise (with similar spectral characteristics and equivalent acoustic energy). The changes in the DPOAE amplitude growth functions measured in both conditioned groups after the subsequent high-level exposure were then compared to the amplitude growth functions measured in animals exposed only to the traumatizing exposure. The results of this series of experiments should agree with the previous reports which demonstrate that prior conditioning of the auditory system provides protection against later damaging exposures (Canlon et al, 1988; Campo et al., 1991). More importantly, the results should demonstrate that a difference exists in the amount of protection afforded by the two conditioning exposure schedules. Specifically, the periods of rest during the interrupted exposure might allow partial recovery thus providing additional protection to the auditory system.

Guinea pigs were randomly assigned to one of six groups (n=14/group). Group assignments were as follows:

**Aged Normal Group (Unexposed)** - The animals in this group were housed and cared for in the Animal Care facility for 7-8 weeks prior to being tested. The level of the ambient noise within this facility was usually between 40 and 50 dB SPL (A-scale). However, during a ½ hour period each day when the cages were being cleaned, this level could be as high as 80 to 90 dB SPL (A-scale).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Continuous Conditioning Group** - The animals in this group were exposed continuously for 11 days to an 89 dB SPL (A-scale) octave band noise (1-2 kHz). These animals were tested within 2 hours after their removal from the noise exposure booth. This 2 hours represented the time needed for surgical manipulation (approximately 1½ hours) plus a ½ hour recovery period from the surgery.

**Interrupted Conditioning Group** - The animals in this group were exposed to a 95 dB SPL (A-scale) octave band noise (1-2 kHz) 6 hours per day for 11 days (6 hrs "on"/18 hrs "off"). These animals were tested within 2 hours after their removal from the noise exposure booth. This 2 hours represented the time needed for surgical manipulation (approximately 1½ hours) plus a ½ hour recovery period from the surgery.

**Continuous Conditioning, then Blast Group** - The animals in this group were exposed continuously for 11 days to an 89 dB SPL octave band noise (1-2 kHz), given 1 week to recover at Louisiana State University Medical Center's Animal Care facility, exposed continuously to a 105 dB SPL (A-scale, 1-2 kHz) for 3 days, and then allowed to recover for 4 weeks in the Animal Care facility before being tested.

**Interrupted Conditioning, then Blast Group** - The animals in this group were exposed 6 hours per day for 11 days to a 95 dB SPL octave band noise (1-2 kHz; 6 hours "on"/18 hours "off"), given 1 week to recover at Louisiana

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

State University Medical Center's Animal Care facility, exposed continuously to a 105 dB SPL (A-scale, 1-2 kHz) for 3 days, and then allowed to recover for 4 weeks in the Animal Care facility before being tested.

**Control/Blast Only Group** - The animals in this group were exposed only to the 105 dB SPL (A-scale, 1-2 kHz) for 3 days, and then allowed to recover for 4 weeks in the Animal Care facility before being tested. The amount of time these animals spent in the facility prior to exposure was such that the time required to condition the animals in the other groups (11 days) and allow them to recover (1 week) were equivalent.

The design of this experiment is illustrated in Table 2.

### 3.7 Data management and analysis

Statistical analysis of the data was performed using SigmaStat® Statistical Software (Version 2.0 for Windows® 95, NT, & 3.1; Jandel Scientific Corporation). The response measurements (DPOAE amplitude growth functions) of all exposure groups were analyzed using a between-group, three-way (exposure group x frequency x primary level) analysis of variance (ANOVA) procedure. The Tukey multiple comparisons (post hoc) test was performed when significant differences were found. P values less than 0.05 were considered statistically significant.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 2.** Experimental design

| | | | |
|---|---|---|---|
| E | R | $X_1$ | O |
| E | R | $X_2$ | O |
| C | R | $X_3$ | O |

**Abbreviations:**

E = Experimental group (n=14/group)

C = Control group (n=14)

R = Subjects will be randomly assigned

**Treatments:**

$X_1$ = Continuous Conditioning, then Blast Group

$X_2$ = Interrupted Conditioning, then Blast Group

$X_3$ = Control/Blast Only Group

O = Response measurements (DPOAE amplitude growth functions)

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CHAPTER 4

# RESULTS

The response measurements (DPOAE amplitude growth functions) of all exposure groups are presented in Appendix A (individual animal data) and Appendix B (mean ± standard error (S.E.) data). Data were analyzed using a three-way (Exposure Group x Frequency x Intensity) ANOVA. Focus was placed on answering two major experimental questions: (1) What was the effect of the sound conditioning protocols (continuous vs. interrupted) on DPOAE amplitude growth functions; and (2) Did prior sound conditioning provide protection against the damaging effects of the traumatizing noise exposure, and if so, was one sound conditioning protocol more effective?

## 4.1 Effects of the sound conditioning exposure protocols on DPOAE responses

The DPOAE amplitude growth functions shown in Figure 2 (a-i) represent the average responses (mean ± S.E.; n=14) of the Continuous Conditioning Group (open down-triangles) and the Interrupted Conditioning Group (open circles). These are plotted in contrast with the average responses (mean ± S.E.; n=14) of the Aged Normal Group (filled circles) to demonstrate the effect of both sound conditioning protocols on normal DPOAE responses and to compare the effects of the two different schedules of conditioning noise.

All main effects (Group, Frequency, Intensity) and interactions of this analysis were statistically



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

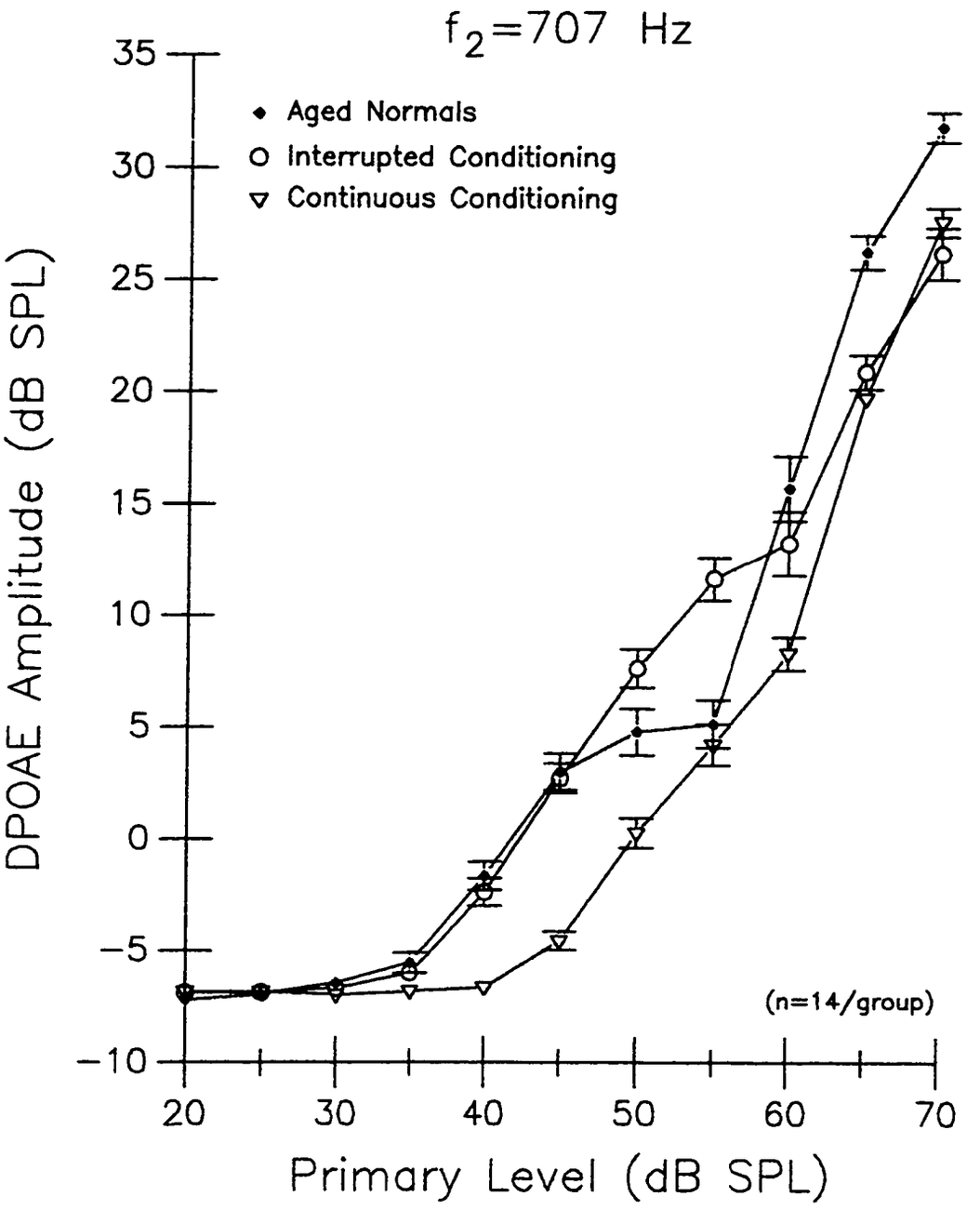


**Figure 2a.** The effect of sound conditioning on DPOAE responses at $f_2$ = 707 Hz. DPOAE amplitude growth functions obtained from the Continuous Conditioning Group (n=14; open down-triangles) and the Interrupted Conditioning Group (n=14; open circles) are plotted along with the functions of the Aged Normal Group (n=14; closed circles). Data are presented as mean DPOAE amplitude ± S.E. as a function of primary level (20-70 dB SPL).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

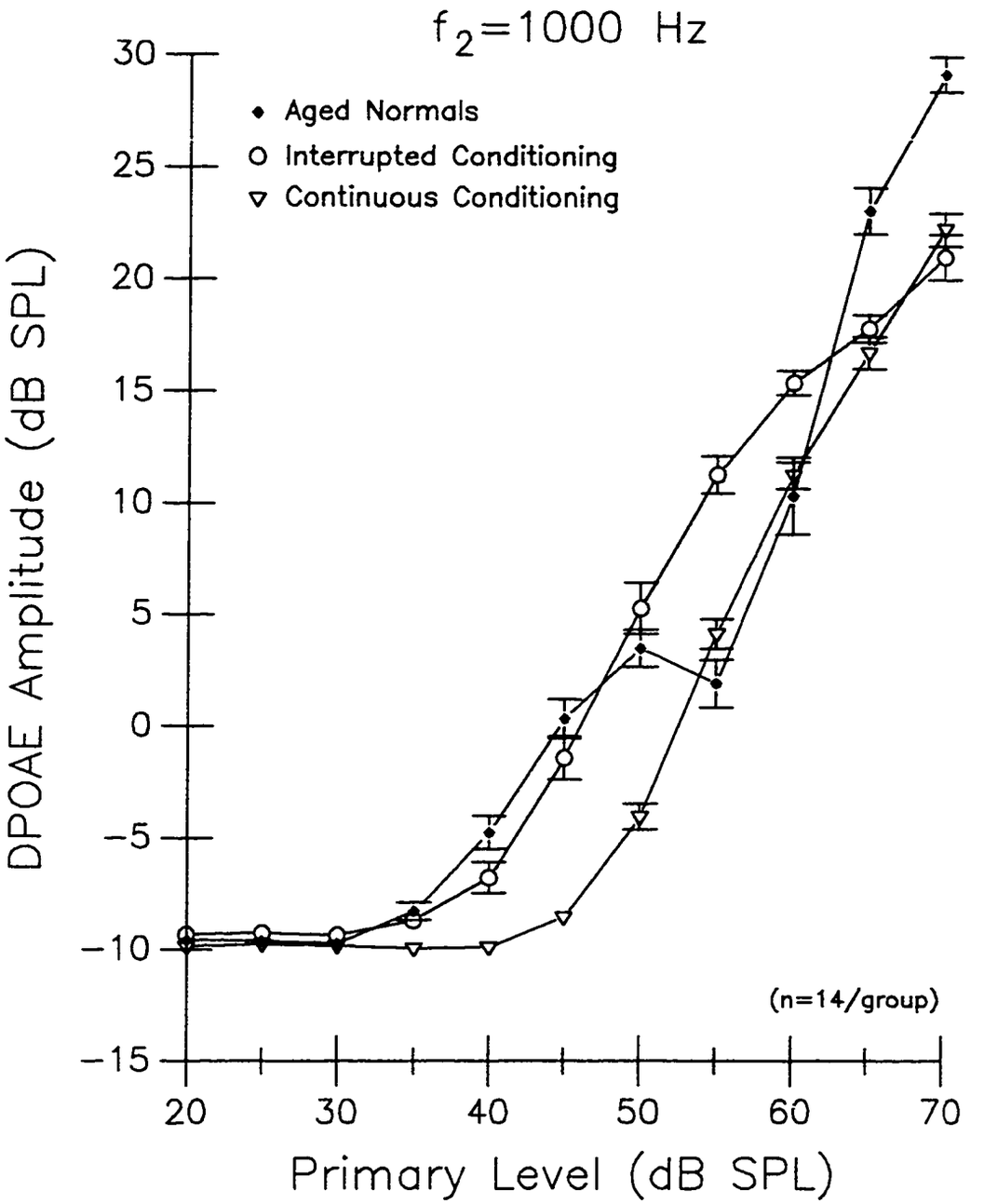


**Figure 2b.** The effect of sound conditioning on DPOAE responses at $f_2$ = 1000 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

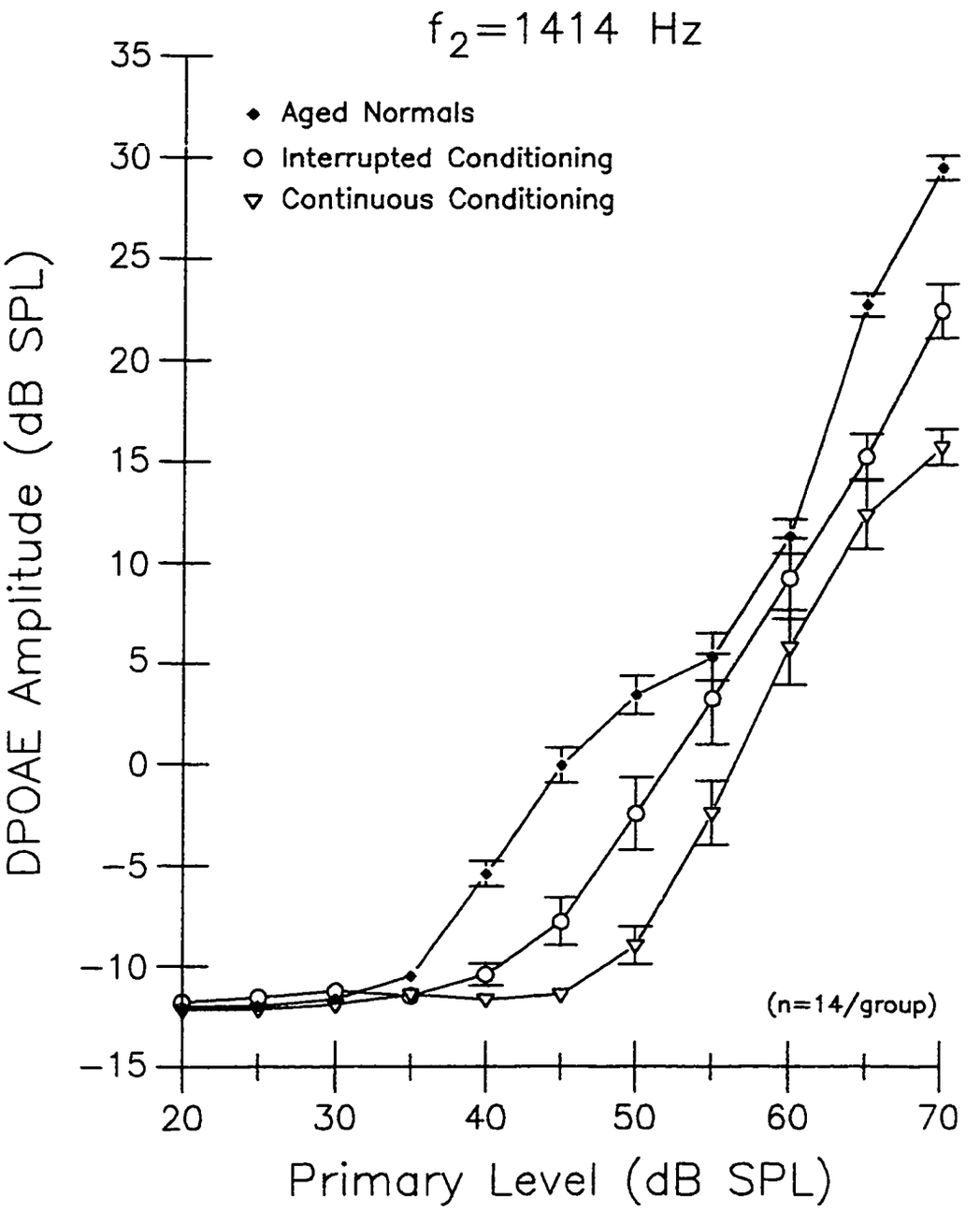


**Figure 2c.** The effect of sound conditioning on DPOAE responses at $f_2$ = 1414 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

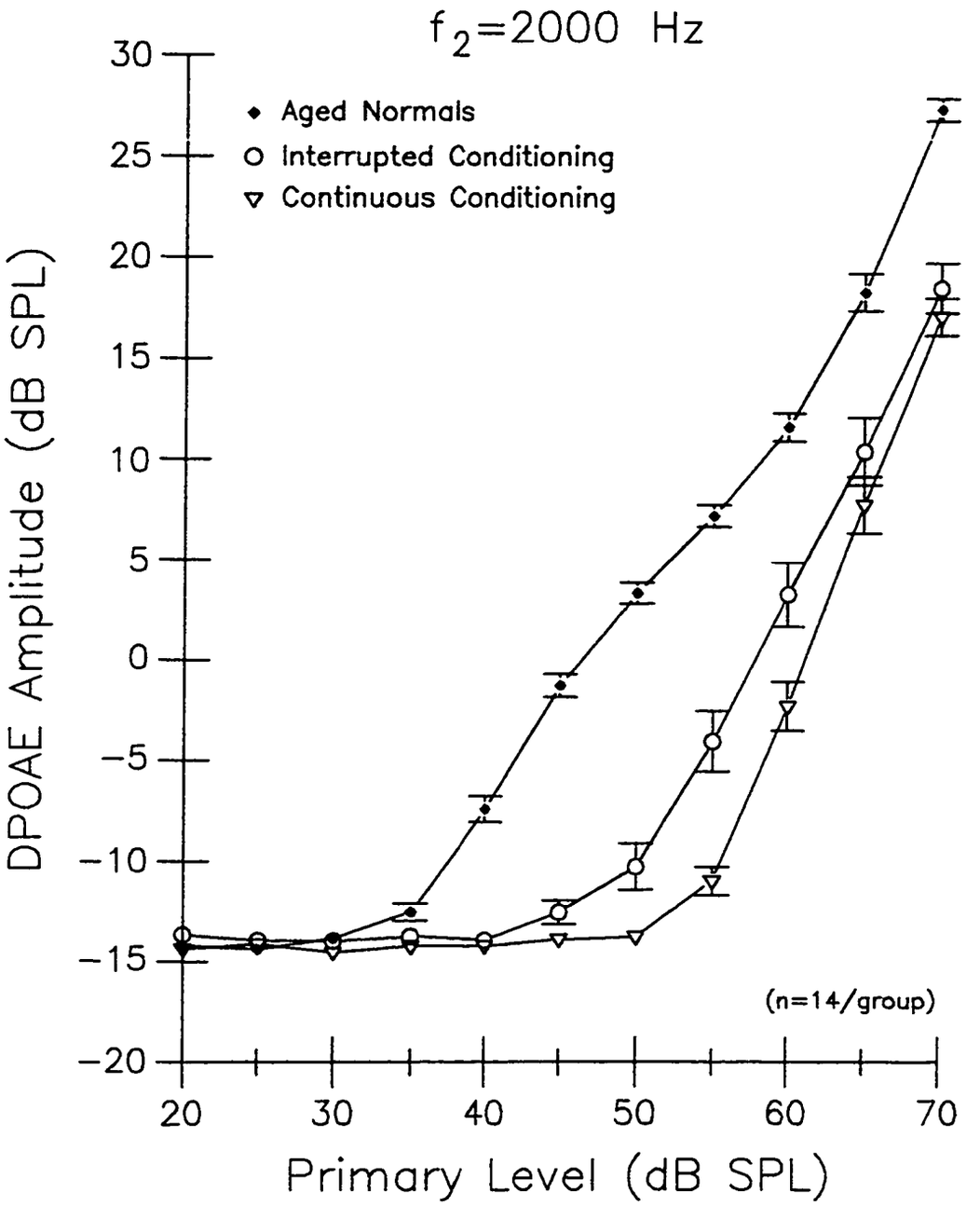


**Figure 2d.** The effect of sound conditioning on DPOAE responses at $f_2$ = 2000 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

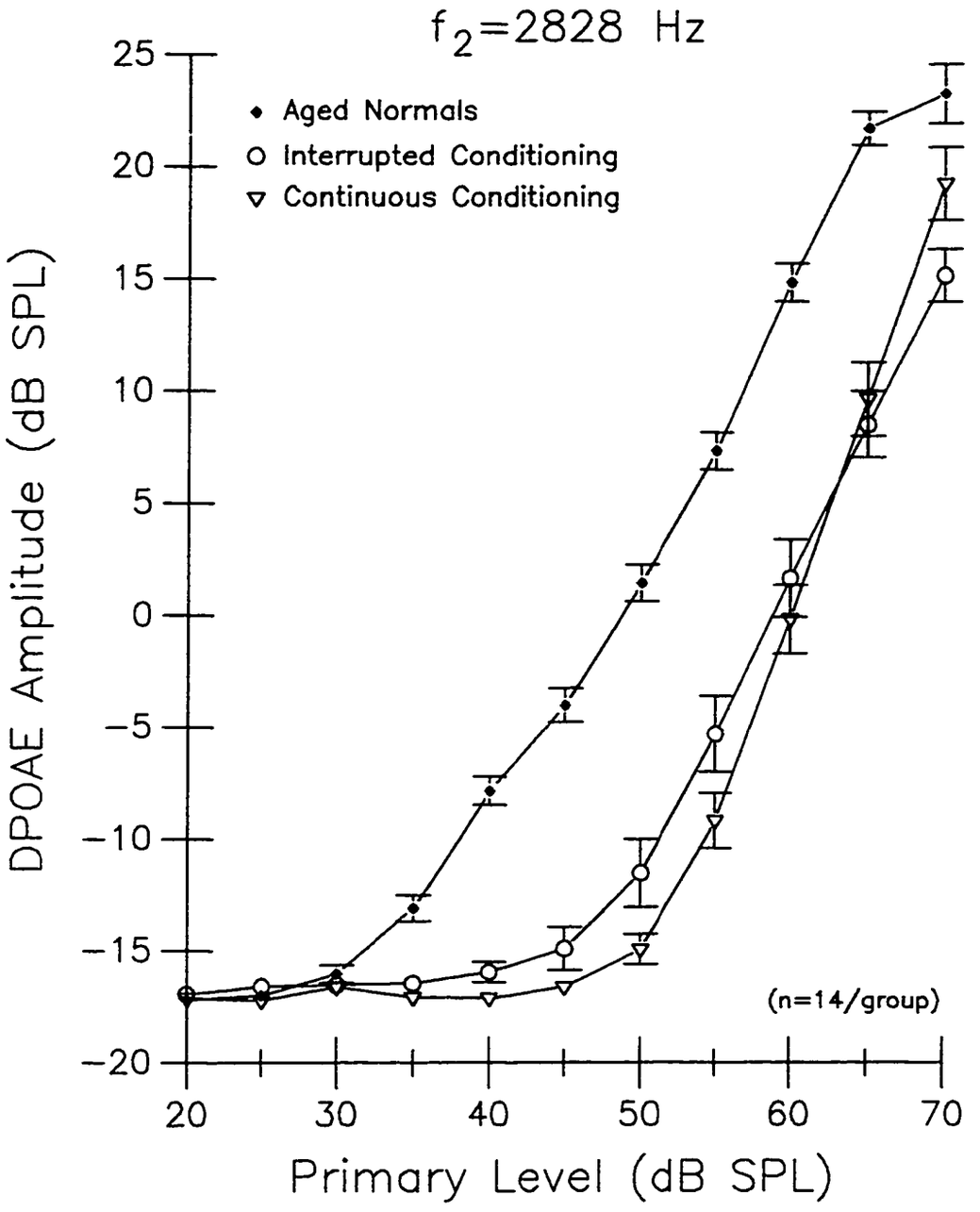


**Figure 2e.** The effect of sound conditioning on DPOAE responses at $f_2$ = 2828 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

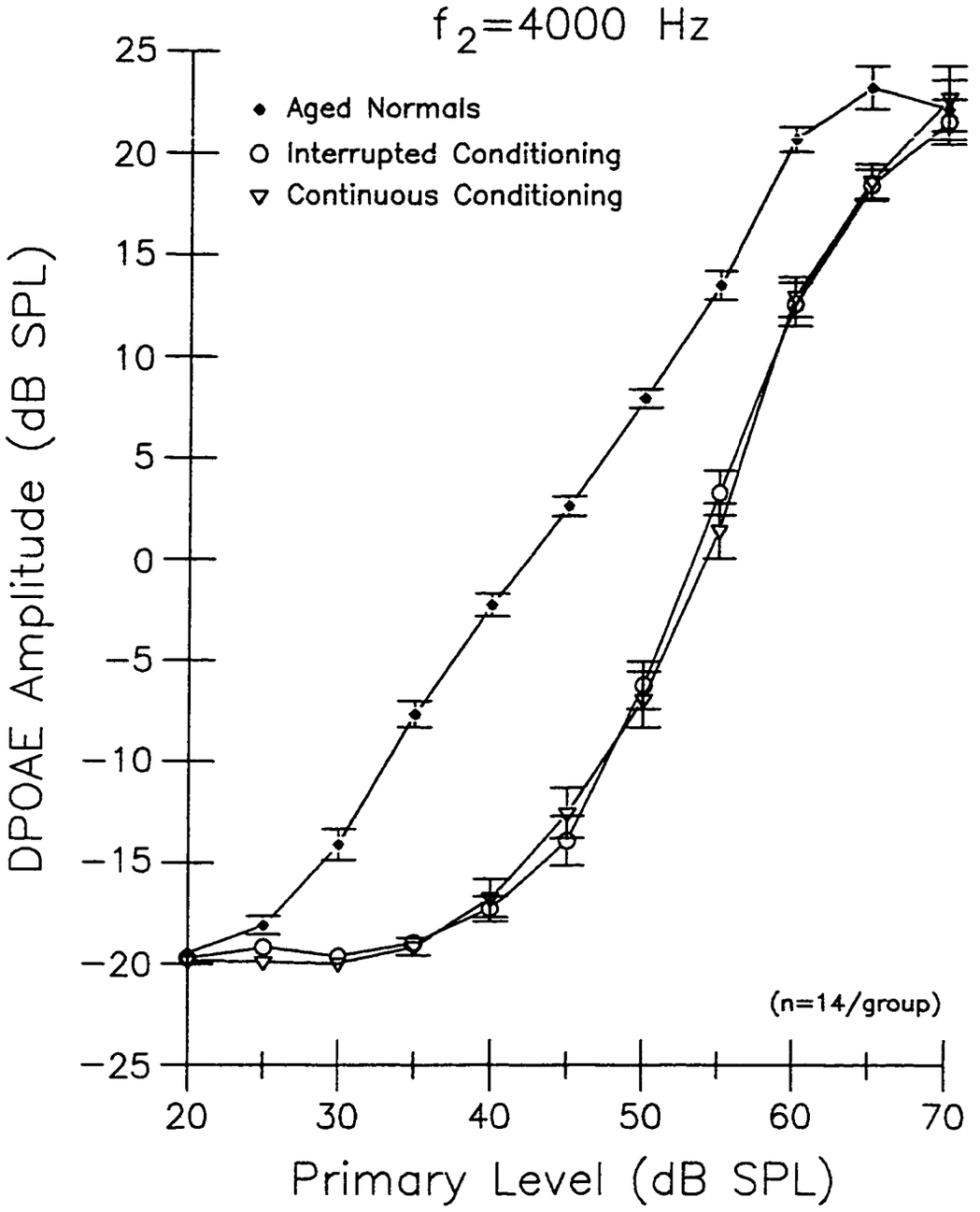


**Figure 2f.** The effect of sound conditioning on DPOAE responses at $f_2$ = 4000 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

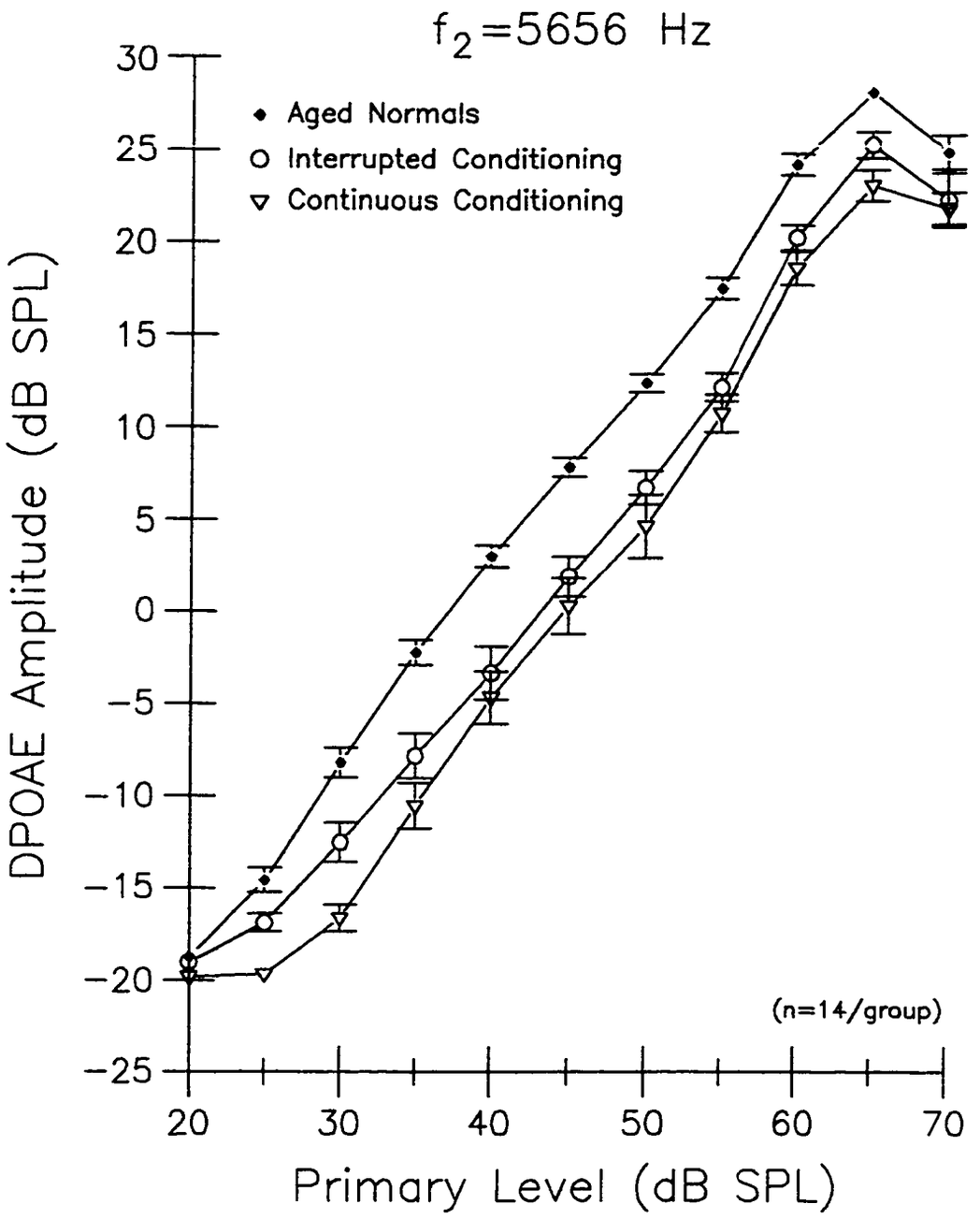


**Figure 2g.** The effect of sound conditioning on DPOAE responses at $f_2$ = 5656 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

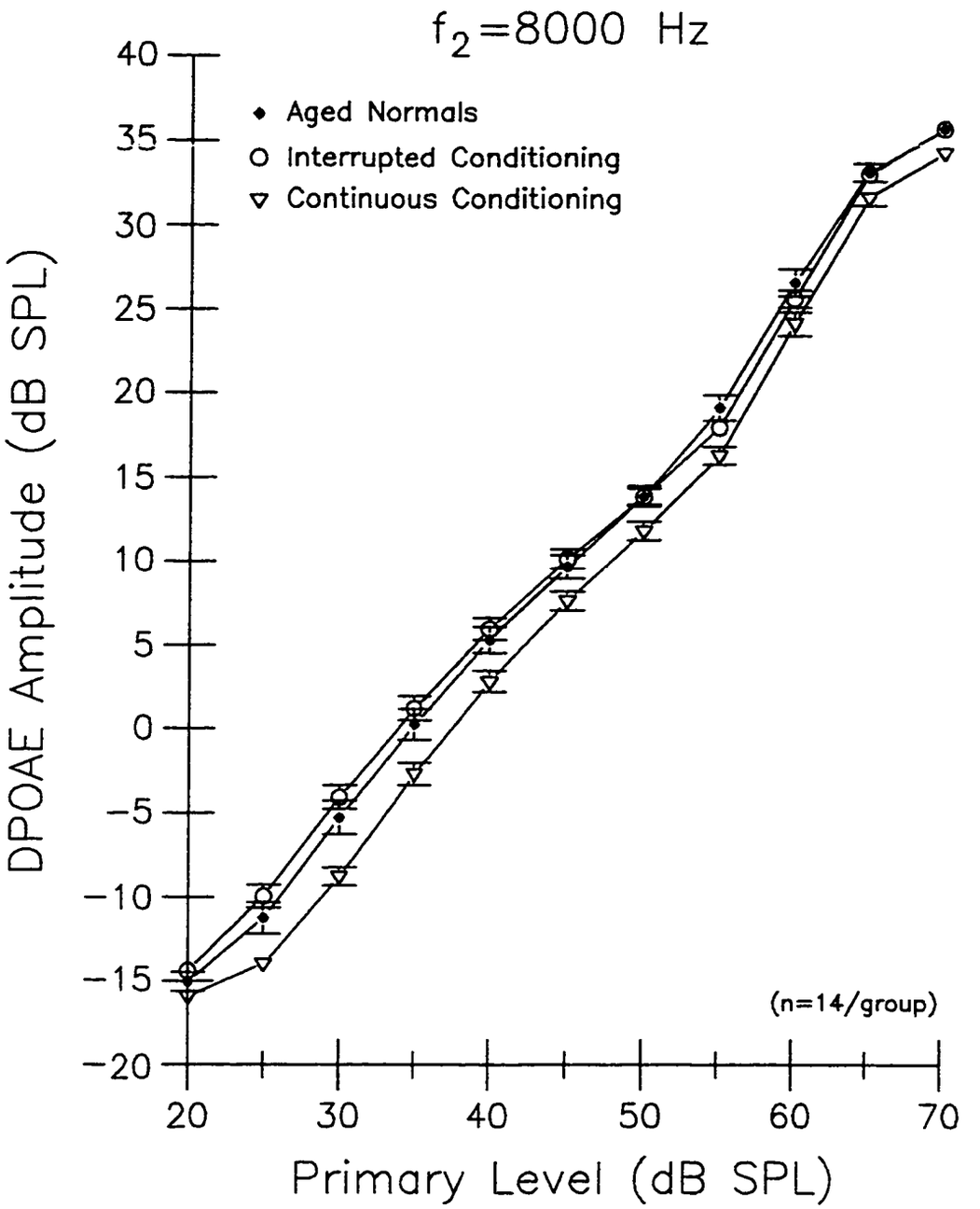


**Figure 2h.** The effect of sound conditioning on DPOAE responses at $f_2$ = 8000 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

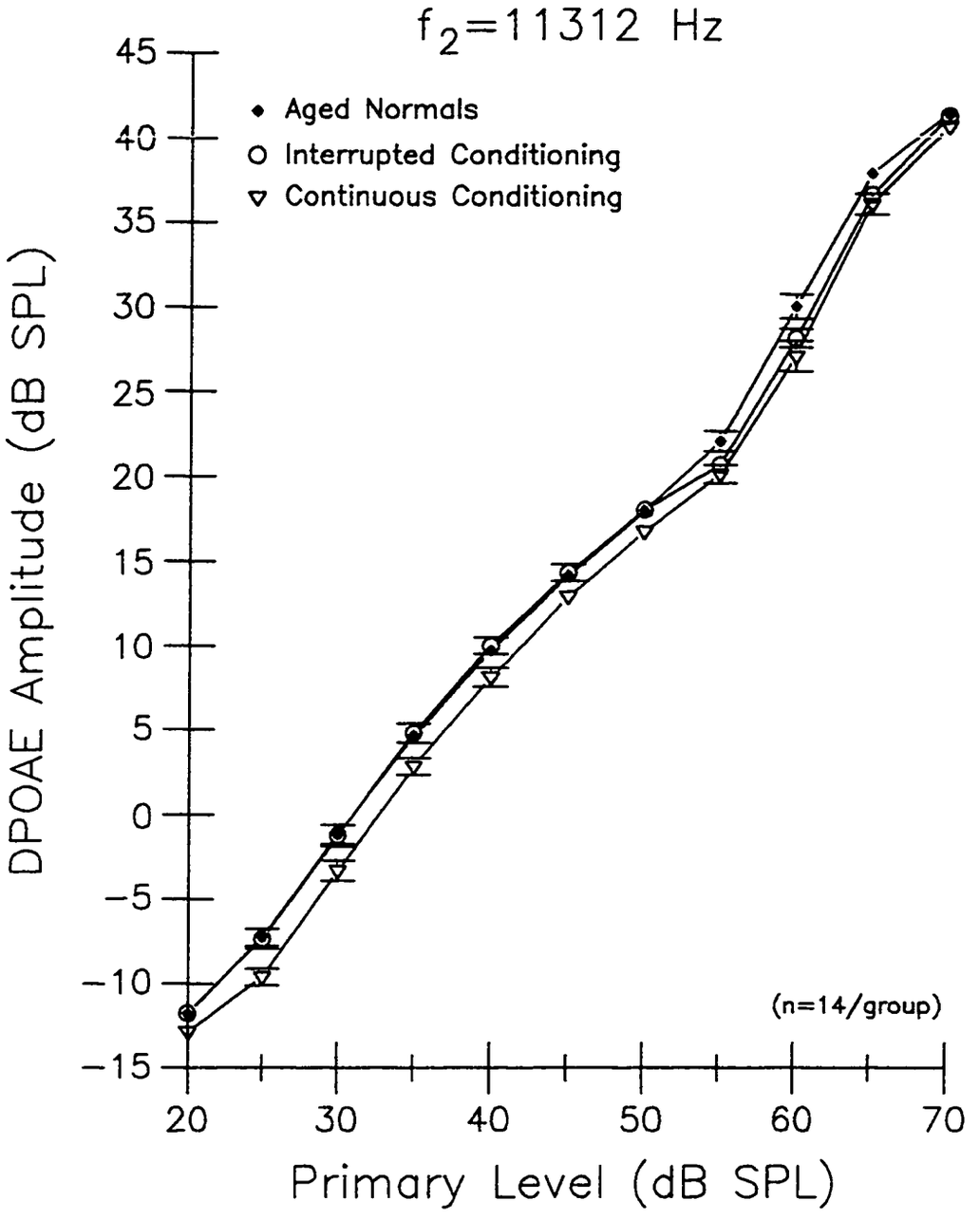


**Figure 2i.** The effect of sound conditioning on DPOAE responses at $f_2$ = 11312 Hz. For additional information, see legend for Figure 2a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

significant ($P<0.001$; see Table 3). When the interactions between the factors were examined more thoroughly, it was found that (1) the effects of the Group x Frequency interaction depended on the intensity level of the primaries; and (2) the effects of the Group x Intensity interaction depended on the frequency of $f_2$. There was not a significant Group x Frequency interaction when the intensity of the primary tones was 20 dB ($P = 1.000$); however, this interaction was significant at all other intensity levels. In addition, there were not significant Group x Intensity interactions when the frequency of $f_2$ was 8000 ($P = 0.826$) and 11312 Hz ($P = 0.997$), whereas significant interactions were found at all other $f_2$ frequencies. Table 4 (a-h) specifies where the significant differences between the exposure groups occurred according to the frequency of $f_2$ and the intensity level of the primary tones.

### 4.2 Effects of the traumatizing noise exposure on the DPOAE responses of unconditioned and sound conditioned animals

The DPOAE amplitude growth functions shown in Figure 3 (a-i) represent the average responses (mean ± S.E.; n=14) of the Blast Only Group (open up-triangles), the Continuous Conditioning then Blast Group (open squares), and the Interrupted Conditioning then Blast Group (open diamonds). These are plotted together to illustrate the effects of the traumatizing noise exposure in both unconditioned and sound conditioned animals.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 3.** Three-way ANOVA Table - Analysis of the effects of the sound conditioning exposure protocols on DPOAE responses.

| Source of Variation | DF | SS | MS | F | P |
|---|---|---|---|---|---|
| Group | 2 | 19841.305 | 9920.653 | 1086.330 | <0.001 |
| Frequency | 8 | 154540.678 | 19317.585 | 2115.312 | <0.001 |
| Intensity | 10 | 753861.025 | 75386.102 | 8254.922 | <0.001 |
| Group x Frequency | 16 | 8121.907 | 507.619 | 55.585 | <0.001 |
| Group x Intensity | 20 | 6185.073 | 309.254 | 33.864 | <0.001 |
| Frequency x Intensity | 80 | 44074.391 | 550.930 | 60.328 | <0.001 |
| Group x Frequency x Intensity | 160 | 11017.196 | 68.857 | 7.540 | <0.001 |
| Residual | 3861 | 35259.658 | 9.132 | | |
| Total | 4157 | 1032901.233 | 248.473 | | |

**Table 4a.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 707 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 40 dB | AGE vs. CON | 5.004 | 3 | 6.195 | Yes |
| | AGE vs. INT | 0.729 | 3 | 0.902 | Yes |
| | INT vs. CON | 4.275 | 3 | 5.293 | Yes |
| | | | | | |
| 45 dB | AGE vs. CON | 7.558 | 3 | 9.358 | Yes |
| | AGE vs. INT | 0.290 | 3 | 0.359 | No |
| | INT vs. CON | 7.268 | 3 | 8.999 | Yes |
| | | | | | |
| 50 dB | INT vs. CON | 7.383 | 3 | 9.141 | Yes |
| | INT vs. AGE | 2.859 | 3 | 3.540 | Yes |
| | AGE vs. CON | 4.524 | 3 | 5.601 | Yes |
| | | | | | |
| 55 dB | INT vs. CON | 7.446 | 3 | 9.220 | Yes |
| | INT vs. AGE | 6.524 | 3 | 8.077 | Yes |
| | AGE vs. CON | 0.923 | 3 | 1.143 | Yes |
| | | | | | |
| 60 dB | AGE vs. CON | 7.415 | 3 | 9.181 | Yes |
| | AGE vs. INT | 2.470 | 3 | 3.058 | Yes |
| | INT vs. CON | 4.945 | 3 | 6.123 | Yes |
| | | | | | |
| 65 dB | AGE vs. CON | 6.526 | 3 | 8.080 | Yes |
| | AGE vs. INT | 5.354 | 3 | 6.629 | Yes |
| | INT vs. CON | 1.171 | 3 | 1.450 | Yes |
| | | | | | |
| 70 dB | AGE vs. INT | 5.616 | 3 | 6.953 | Yes |
| | AGE vs. CON | 4.223 | 3 | 5.229 | Yes |
| | CON vs. INT | 1.393 | 3 | 1.725 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4b.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 1000 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 40 dB | AGE vs. CON | 5.143 | 3 | 6.368 | Yes |
| | AGE vs. INT | 2.020 | 3 | 2.501 | Yes |
| | INT vs. CON | 3.123 | 3 | 3.867 | Yes |
| | | | | | |
| 45 dB | AGE vs. CON | 8.882 | 3 | 10.997 | Yes |
| | AGE vs. INT | 1.744 | 3 | 2.160 | Yes |
| | INT vs. CON | 7.138 | 3 | 8.838 | Yes |
| | | | | | |
| 50 dB | INT vs. CON | 9.345 | 3 | 11.571 | Yes |
| | INT vs. AGE | 1.792 | 3 | 2.219 | Yes |
| | AGE vs. CON | 7.553 | 3 | 9.352 | Yes |
| | | | | | |
| 55 dB | INT vs. AGE | 9.379 | 3 | 11.612 | Yes |
| | INT vs. CON | 7.143 | 3 | 8.844 | Yes |
| | CON vs. AGE | 2.236 | 3 | 2.768 | Yes |
| | | | | | |
| 60 dB | INT vs. AGE | 5.061 | 3 | 6.266 | Yes |
| | INT vs. CON | 4.143 | 3 | 5.129 | Yes |
| | CON vs. AGE | 0.918 | 3 | 1.136 | Yes |
| | | | | | |
| 65 dB | AGE vs. CON | 6.331 | 3 | 7.838 | Yes |
| | AGE vs. INT | 5.256 | 3 | 6.508 | Yes |
| | INT vs. CON | 1.074 | 3 | 1.330 | Yes |
| | | | | | |
| 70 dB | AGE vs. INT | 8.145 | 3 | 10.085 | Yes |
| | AGE vs. CON | 6.912 | 3 | 8.558 | Yes |
| | CON vs. INT | 1.233 | 3 | 1.526 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4c.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 1414 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 40 dB | AGE vs. CON | 6.264 | 3 | 7.755 | Yes |
| | AGE vs. INT | 5.008 | 3 | 6.201 | Yes |
| | INT vs. CON | 1.256 | 3 | 1.555 | Yes |
| | | | | | |
| 45 dB | AGE vs. CON | 11.378 | 3 | 14.088 | Yes |
| | AGE vs. INT | 7.756 | 3 | 9.604 | Yes |
| | INT vs. CON | 3.621 | 3 | 4.484 | Yes |
| | | | | | |
| 50 dB | AGE vs. CON | 12.416 | 3 | 15.373 | Yes |
| | AGE vs. INT | 5.889 | 3 | 7.291 | Yes |
| | INT vs. CON | 6.527 | 3 | 8.082 | Yes |
| | | | | | |
| 55 dB | AGE vs. CON | 7.759 | 3 | 9.606 | Yes |
| | AGE vs. INT | 2.099 | 3 | 2.599 | Yes |
| | INT vs. CON | 5.659 | 3 | 7.007 | Yes |
| | | | | | |
| 60 dB | AGE vs. CON | 5.525 | 3 | 6.841 | Yes |
| | AGE vs. INT | 2.114 | 3 | 2.617 | Yes |
| | INT vs. CON | 3.411 | 3 | 4.224 | Yes |
| | | | | | |
| 65 dB | AGE vs. CON | 10.359 | 3 | 12.826 | Yes |
| | AGE vs. INT | 7.484 | 3 | 9.267 | Yes |
| | INT vs. CON | 2.874 | 3 | 3.559 | Yes |
| | | | | | |
| 70 dB | AGE vs. CON | 13.769 | 3 | 17.048 | Yes |
| | AGE vs. INT | 7.061 | 3 | 8.743 | Yes |
| | INT vs. CON | 6.707 | 3 | 8.304 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4d.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 2000 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 40 dB | AGE vs. CON | 6.802 | 3 | 8.422 | Yes |
| | AGE vs. INT | 6.526 | 3 | 8.081 | Yes |
| | INT vs. CON | 0.276 | 3 | 0.341 | No |
| | | | | | |
| 45 dB | AGE vs. CON | 12.636 | 3 | 15.645 | Yes |
| | AGE vs. INT | 11.275 | 3 | 13.960 | Yes |
| | INT vs. CON | 1.361 | 3 | 1.685 | Yes |
| | | | | | |
| 50 dB | AGE vs. CON | 17.074 | 3 | 21.140 | Yes |
| | AGE vs. INT | 13.582 | 3 | 16.817 | Yes |
| | INT vs. CON | 3.491 | 3 | 4.323 | Yes |
| | | | | | |
| 55 dB | AGE vs. CON | 18.197 | 3 | 22.531 | Yes |
| | AGE vs. INT | 11.223 | 3 | 13.896 | Yes |
| | INT vs. CON | 6.974 | 3 | 8.635 | Yes |
| | | | | | |
| 60 dB | AGE vs. CON | 13.898 | 3 | 17.208 | Yes |
| | AGE vs. INT | 8.347 | 3 | 10.335 | Yes |
| | INT vs. CON | 5.551 | 3 | 6.873 | Yes |
| | | | | | |
| 65 dB | AGE vs. CON | 10.544 | 3 | 13.055 | Yes |
| | AGE vs. INT | 7.884 | 3 | 9.761 | Yes |
| | INT vs. CON | 2.660 | 3 | 3.293 | Yes |
| | | | | | |
| 70 dB | AGE vs. CON | 10.265 | 3 | 12.710 | Yes |
| | AGE vs. INT | 8.836 | 3 | 10.940 | Yes |
| | INT vs. CON | 1.429 | 3 | 1.770 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4e.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 2828 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 40 dB | AGE vs. CON | 9.269 | 3 | 11.476 | Yes |
| | AGE vs. INT | 8.093 | 3 | 10.020 | Yes |
| | INT vs. CON | 1.176 | 3 | 1.456 | Yes |
| | | | | | |
| 45 dB | AGE vs. CON | 12.622 | 3 | 15.628 | Yes |
| | AGE vs. INT | 10.896 | 3 | 13.491 | Yes |
| | INT vs. CON | 1.726 | 3 | 2.138 | Yes |
| | | | | | |
| 50 dB | AGE vs. CON | 16.388 | 3 | 20.291 | Yes |
| | AGE vs. INT | 12.972 | 3 | 16.062 | Yes |
| | INT vs. CON | 3.416 | 3 | 4.229 | Yes |
| | | | | | |
| 55 dB | AGE vs. CON | 16.540 | 3 | 20.479 | Yes |
| | AGE vs. INT | 12.654 | 3 | 15.667 | Yes |
| | INT vs. CON | 3.886 | 3 | 4.812 | Yes |
| | | | | | |
| 60 dB | AGE vs. CON | 15.026 | 3 | 18.604 | Yes |
| | AGE vs. INT | 13.200 | 3 | 16.344 | Yes |
| | INT vs. CON | 1.826 | 3 | 2.261 | Yes |
| | | | | | |
| 65 dB | AGE vs. INT | 13.172 | 3 | 16.309 | Yes |
| | AGE vs. CON | 12.049 | 3 | 14.918 | Yes |
| | CON vs. INT | 1.124 | 3 | 1.391 | Yes |
| | | | | | |
| 70 dB | AGE vs. INT | 8.112 | 3 | 10.044 | Yes |
| | AGE vs. CON | 4.020 | 3 | 4.977 | Yes |
| | CON vs. INT | 4.092 | 3 | 5.067 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4f.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 4000 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 25 dB | AGE vs. CON | 4.665 | 3 | 5.776 | Yes |
| | AGE vs. INT | 3.944 | 3 | 4.883 | Yes |
| | INT vs. CON | 0.721 | 3 | 0.893 | Yes |
| | | | | | |
| 30 dB | AGE vs. CON | 5.883 | 3 | 7.284 | Yes |
| | AGE vs. INT | 5.504 | 3 | 6.814 | Yes |
| | INT vs. CON | 0.379 | 3 | 0.470 | No |
| | | | | | |
| 35 dB | AGE vs. CON | 11.480 | 3 | 14.214 | Yes |
| | AGE vs. INT | 11.306 | 3 | 13.999 | Yes |
| | INT vs. CON | 0.174 | 3 | 0.215 | No |
| | | | | | |
| 40 dB | AGE vs. INT | 15.009 | 3 | 18.584 | Yes |
| | AGE vs. CON | 14.489 | 3 | 17.939 | Yes |
| | CON vs. INT | 0.521 | 3 | 0.645 | No |
| | | | | | |
| 45 dB | AGE vs. INT | 16.601 | 3 | 20.555 | Yes |
| | AGE vs. CON | 15.216 | 3 | 18.840 | Yes |
| | CON vs. INT | 1.385 | 3 | 1.715 | Yes |
| | | | | | |
| 50 dB | AGE vs. CON | 14.889 | 3 | 18.435 | Yes |
| | AGE vs. INT | 14.185 | 3 | 17.563 | Yes |
| | INT vs. CON | 0.704 | 3 | 0.872 | Yes |

(table con'd.)

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 55 dB | AGE vs. CON | 12.111 | 3 | 14.996 | Yes |
| | AGE vs. INT | 10.225 | 3 | 12.660 | Yes |
| | INT vs. CON | 1.886 | 3 | 2.336 | Yes |
| | | | | | |
| 60 dB | AGE vs. INT | 8.098 | 3 | 10.026 | Yes |
| | AGE vs. CON | 7.742 | 3 | 9.586 | Yes |
| | CON vs. INT | 0.356 | 3 | 0.440 | No |
| | | | | | |
| 65 dB | AGE vs. INT | 4.786 | 3 | 5.925 | Yes |
| | AGE vs. CON | 4.591 | 3 | 5.685 | Yes |
| | CON vs. INT | 0.194 | 3 | 0.241 | No |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4g.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 5656 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 25 dB | AGE vs. CON | 5.111 | 3 | 6.329 | Yes |
| | AGE vs. INT | 2.313 | 3 | 2.864 | Yes |
| | INT vs. CON | 2.799 | 3 | 3.465 | Yes |
| | | | | | |
| 30 dB | AGE vs. CON | 8.443 | 3 | 10.454 | Yes |
| | AGE vs. INT | 4.326 | 3 | 5.356 | Yes |
| | INT vs. CON | 4.117 | 3 | 5.098 | Yes |
| | | | | | |
| 35 dB | AGE vs. CON | 8.314 | 3 | 10.294 | Yes |
| | AGE vs. INT | 5.602 | 3 | 6.936 | Yes |
| | INT vs. CON | 2.712 | 3 | 3.358 | Yes |
| | | | | | |
| 40 dB | AGE vs. CON | 7.693 | 3 | 9.525 | Yes |
| | AGE vs. INT | 6.362 | 3 | 7.877 | Yes |
| | INT vs. CON | 1.331 | 3 | 1.648 | Yes |
| | | | | | |
| 45 dB | AGE vs. CON | 7.551 | 3 | 9.349 | Yes |
| | AGE vs. INT | 5.940 | 3 | 7.355 | Yes |
| | INT vs. CON | 1.611 | 3 | 1.994 | Yes |
| | | | | | |
| 50 dB | AGE vs. CON | 7.742 | 3 | 9.586 | Yes |
| | AGE vs. INT | 5.653 | 3 | 6.999 | Yes |
| | INT vs. CON | 2.089 | 3 | 2.587 | Yes |

(table con'd.)

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 55 dB | AGE vs. CON | 6.752 | 3 | 8.360 | Yes |
| | AGE vs. INT | 5.337 | 3 | 6.608 | Yes |
| | INT vs. CON | 1.415 | 3 | 1.752 | Yes |
| | | | | | |
| 60 dB | AGE vs. CON | 5.608 | 3 | 6.943 | Yes |
| | AGE vs. INT | 3.959 | 3 | 4.902 | Yes |
| | INT vs. CON | 1.649 | 3 | 2.041 | Yes |
| | | | | | |
| 65 dB | AGE vs. CON | 5.044 | 3 | 6.246 | Yes |
| | AGE vs. INT | 2.828 | 3 | 3.501 | Yes |
| | INT vs. CON | 2.216 | 6 | 2.744 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 4h.** Summary of the Tukey multiple comparison test results for the main effect of intensity found for DPOAE responses when $f_2$ = 8000 Hz for the Aged Normal (AGE), Continuous (CON) and Interrupted (INT) Conditioning Groups.

| Intensity | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 30 dB | INT vs. CON | 4.719 | 3 | 5.843 | Yes |
| | INT vs. AGE | 1.215 | 3 | 1.504 | Yes |
| | AGE vs. CON | 3.504 | 3 | 4.339 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

All main effects (Group, Frequency, and Intensity) of this analysis were statistically significant (see Table 5). The intergroup differences that were statistically significant are listed in Table 6. When the interactions between the factors were examined more thoroughly, it was found that there was a statistically significant interaction between Group and Frequency. Table 7 specifies where the differences between the exposure groups occurred according to the frequency of $f_2$ when pooling the data across intensity.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

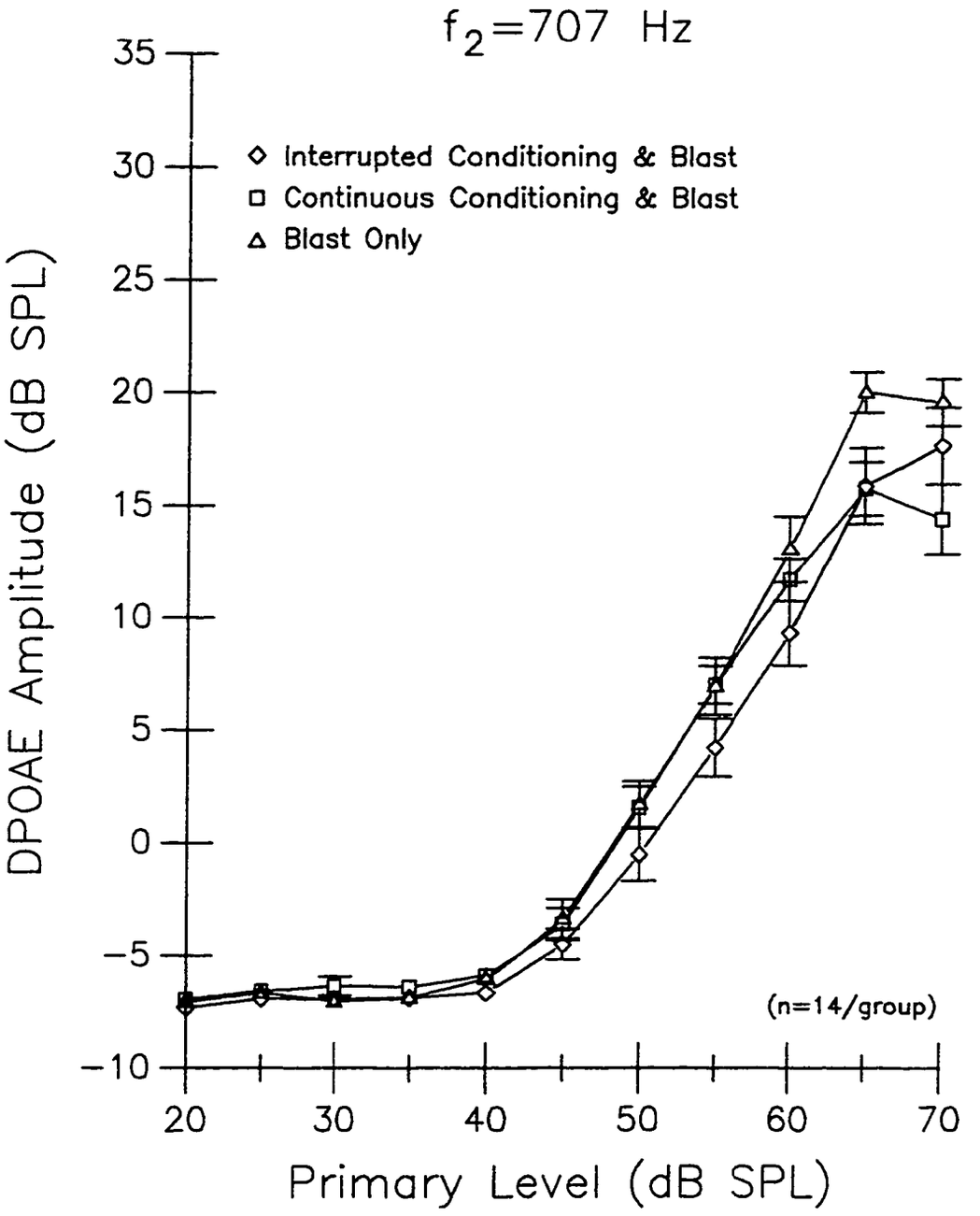


**Figure 3a.** The effect of the traumatizing noise exposure on the DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 707 Hz. The individual plots represent the DPOAE amplitude growth functions obtained from the Blast Only Group (n=14; open up-triangles), the Continuous Conditioning then Blast Group (n=14; open squares), and the Interrupted Conditioning then Blast Group (n=14; open diamonds). Data are presented as mean DPOAE amplitude ± S.E. as a function of primary level (20-70 dB SPL).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

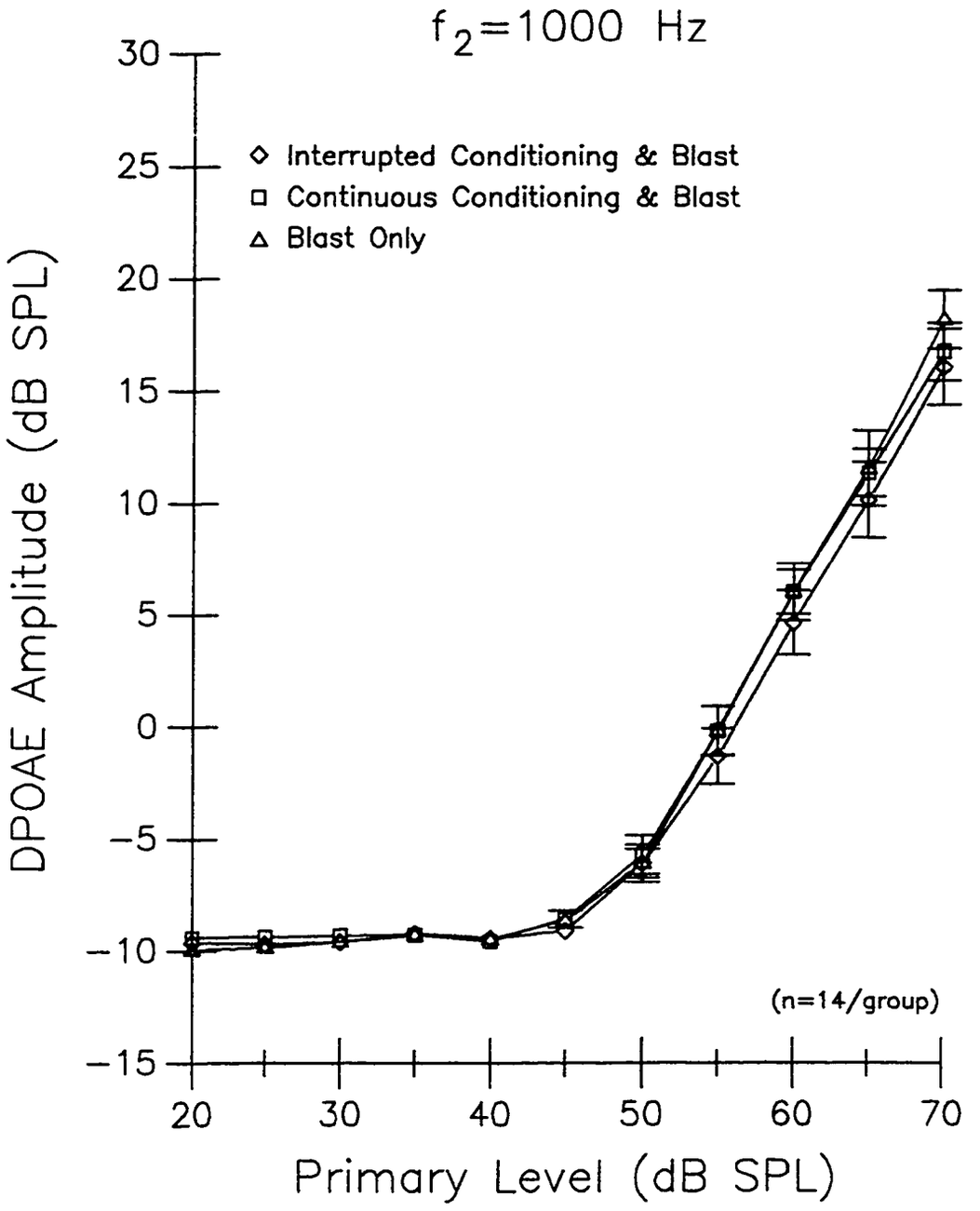


**Figure 3b.** The effect of the traumatizing noise exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 1000 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

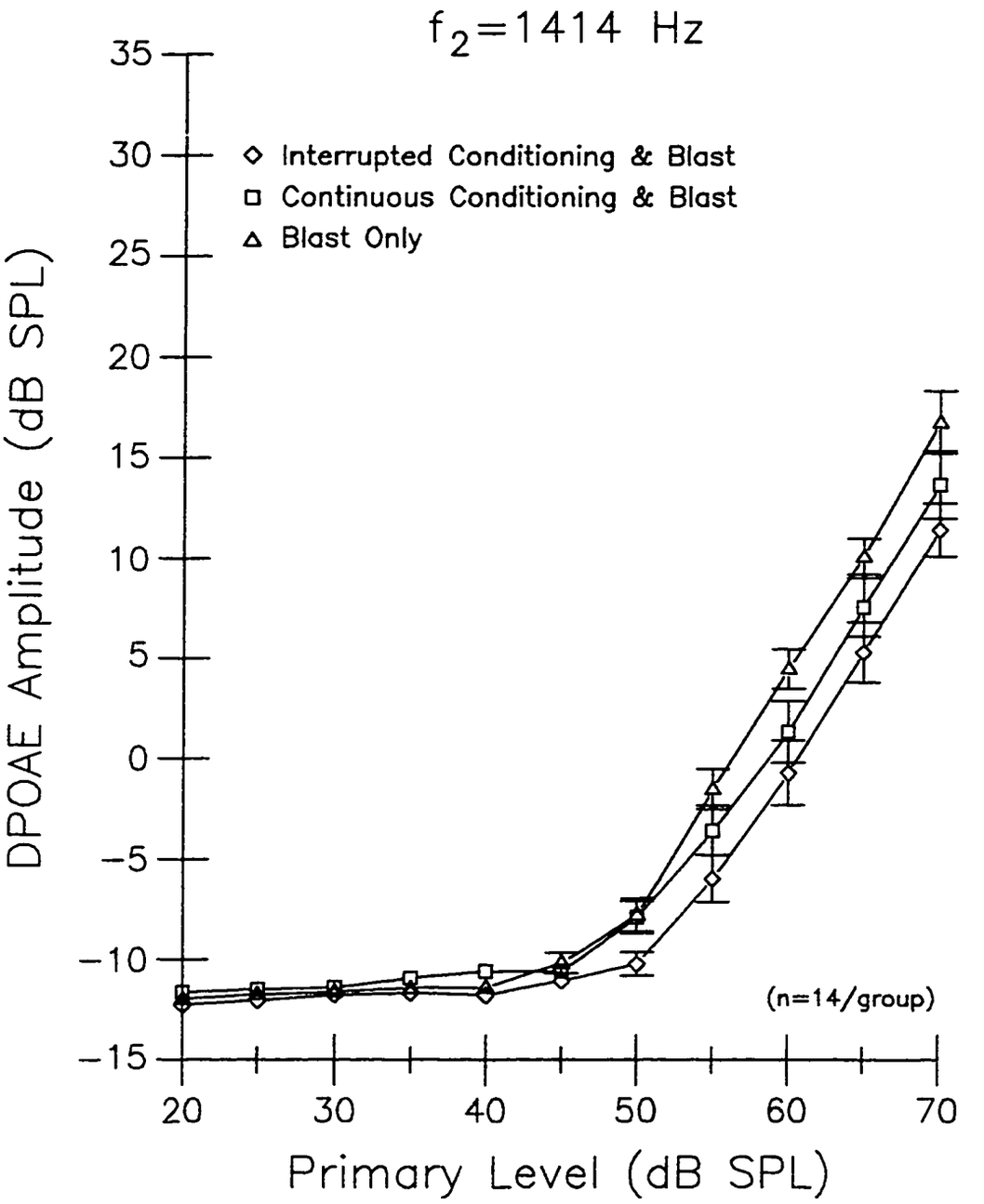


**Figure 3c.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 1414 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

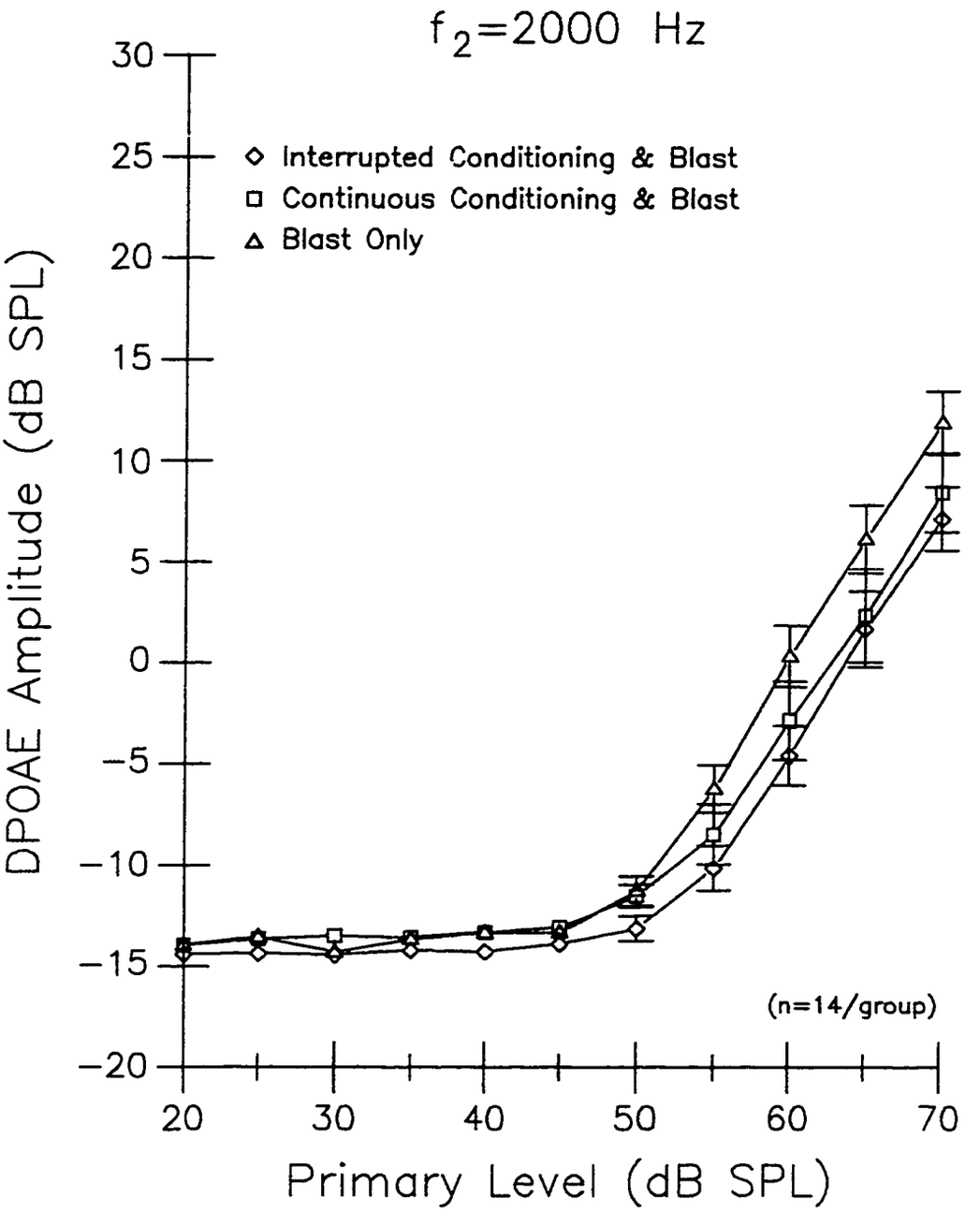


**Figure 3d.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 2000 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

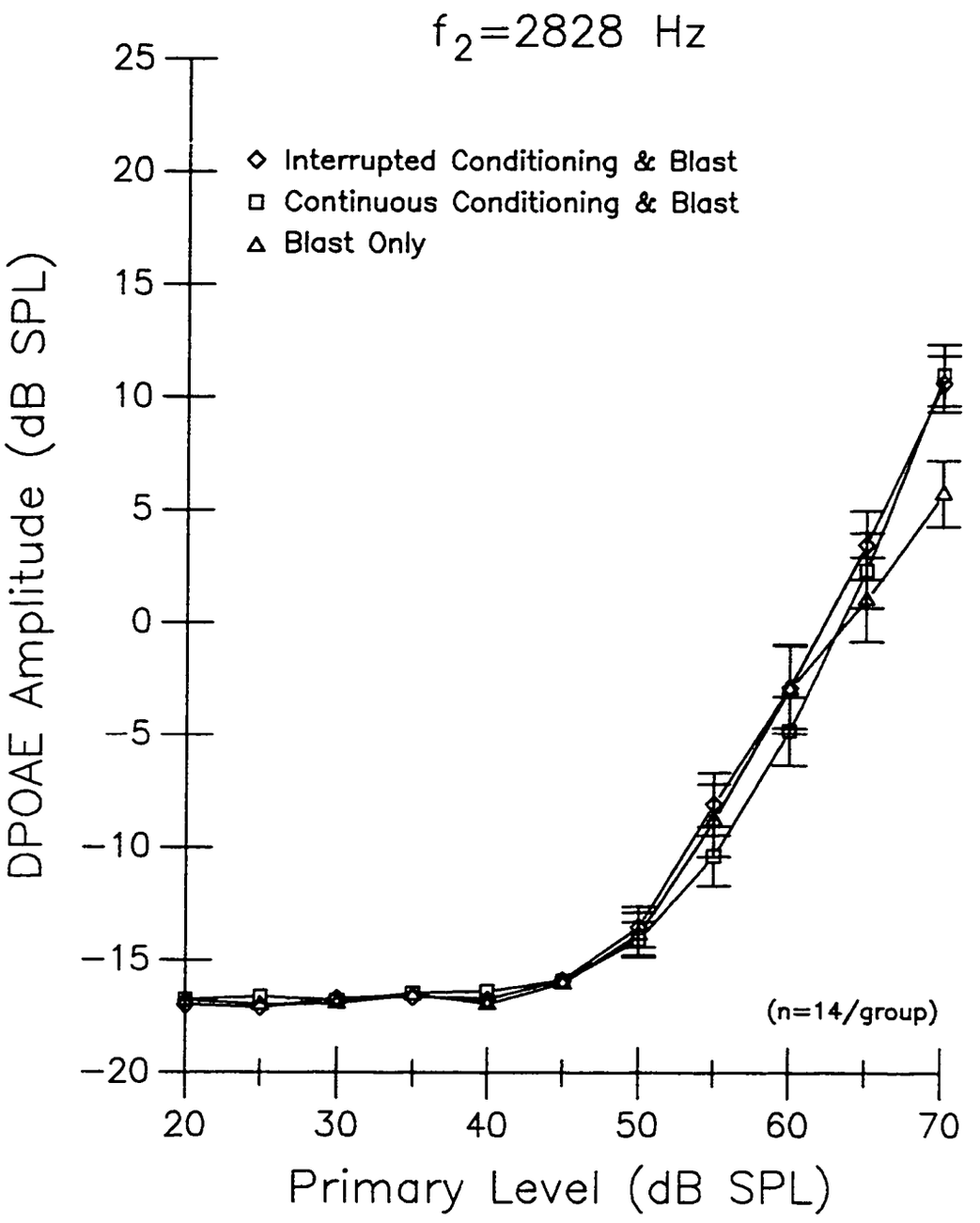


**Figure 3e.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 2828 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

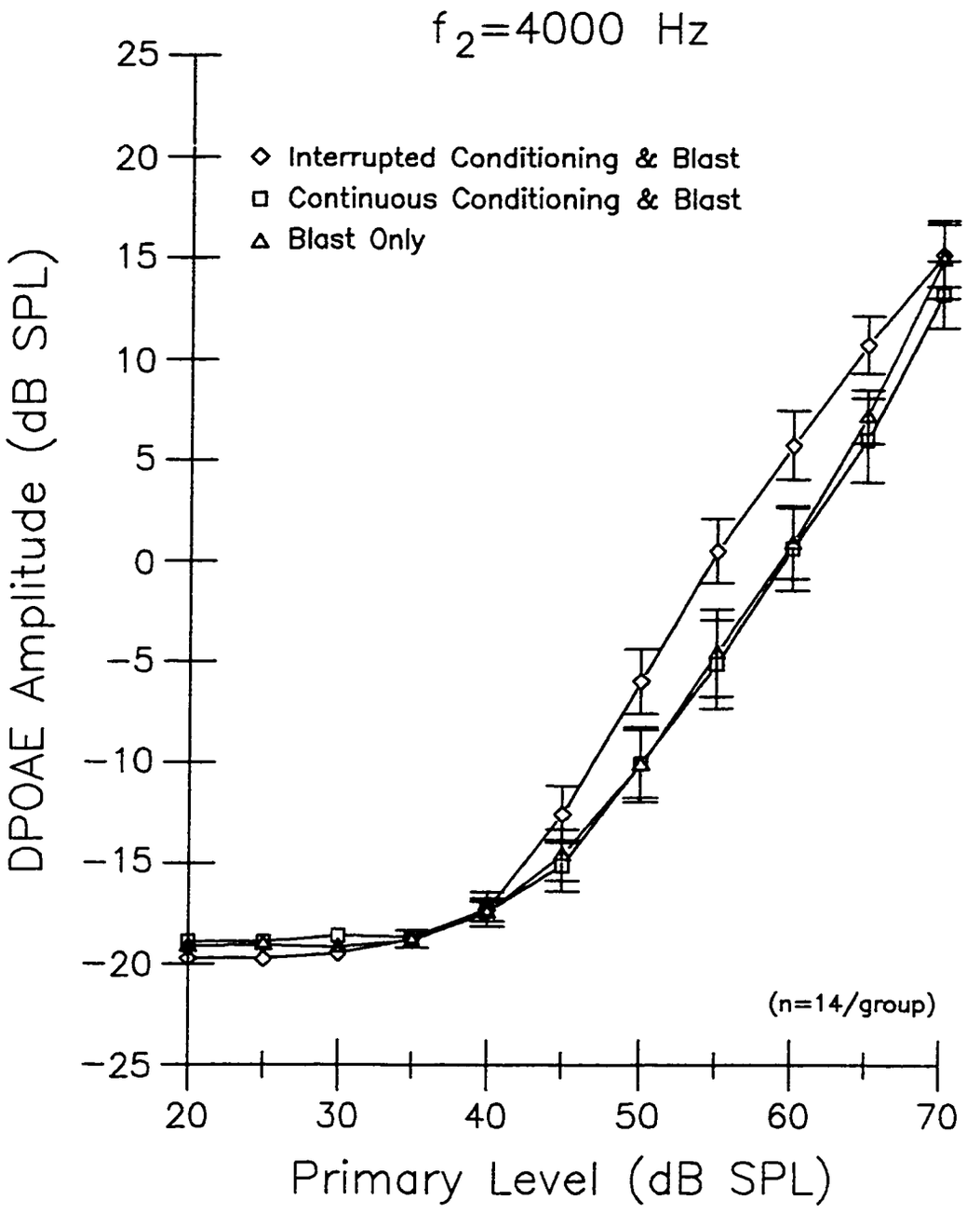


**Figure 3f.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 4000 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

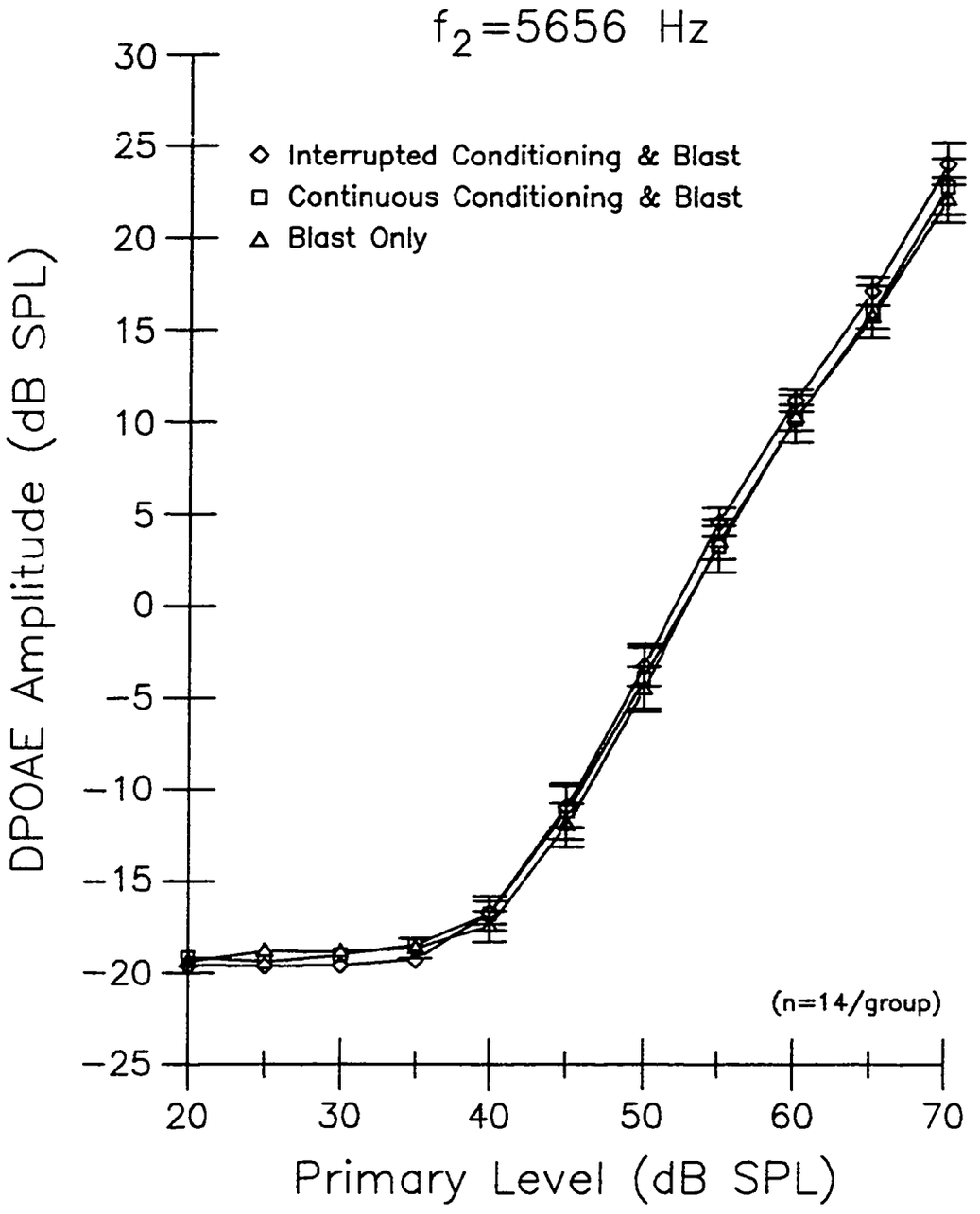


**Figure 3g.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 5656 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

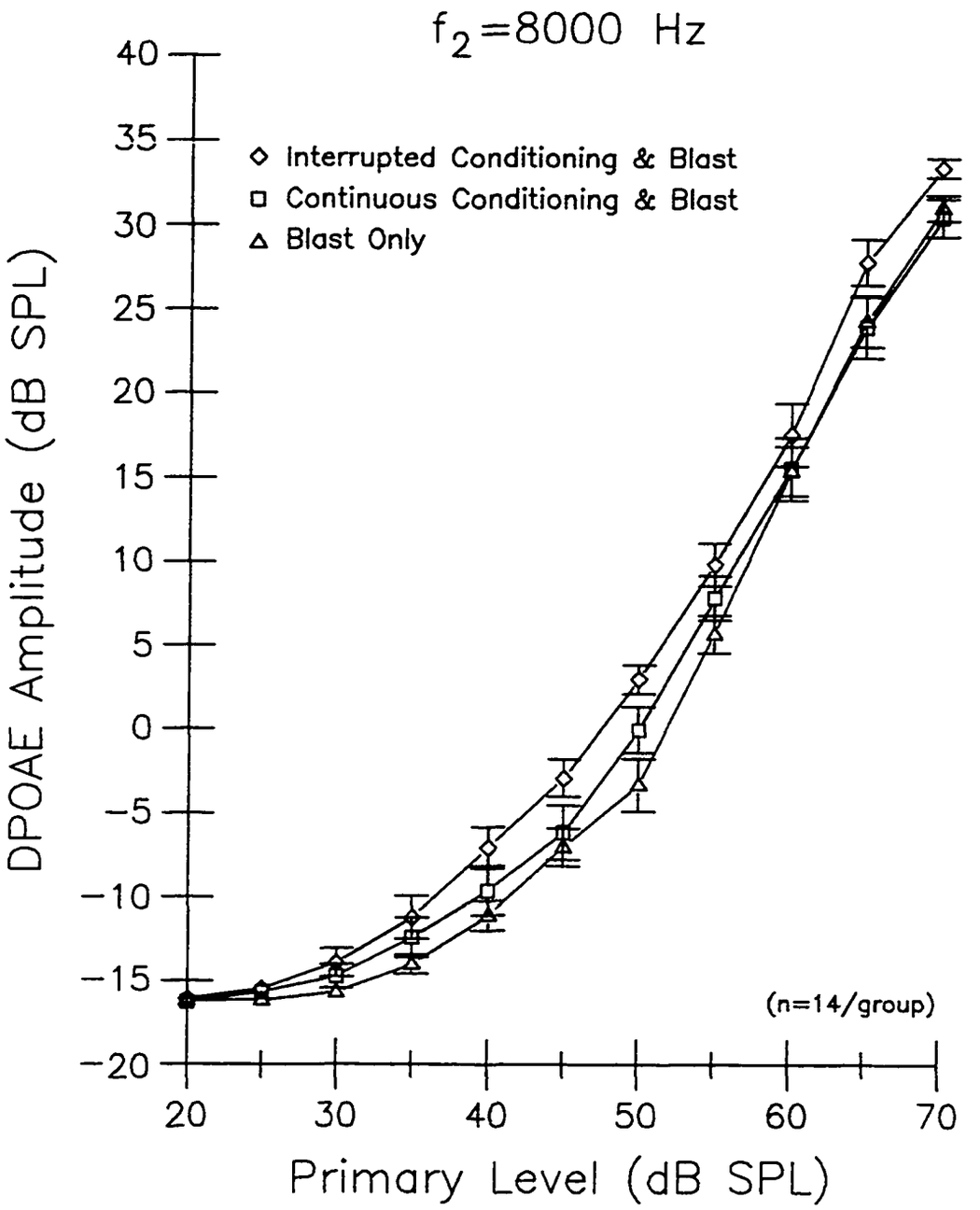


**Figure 3h.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 8000 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

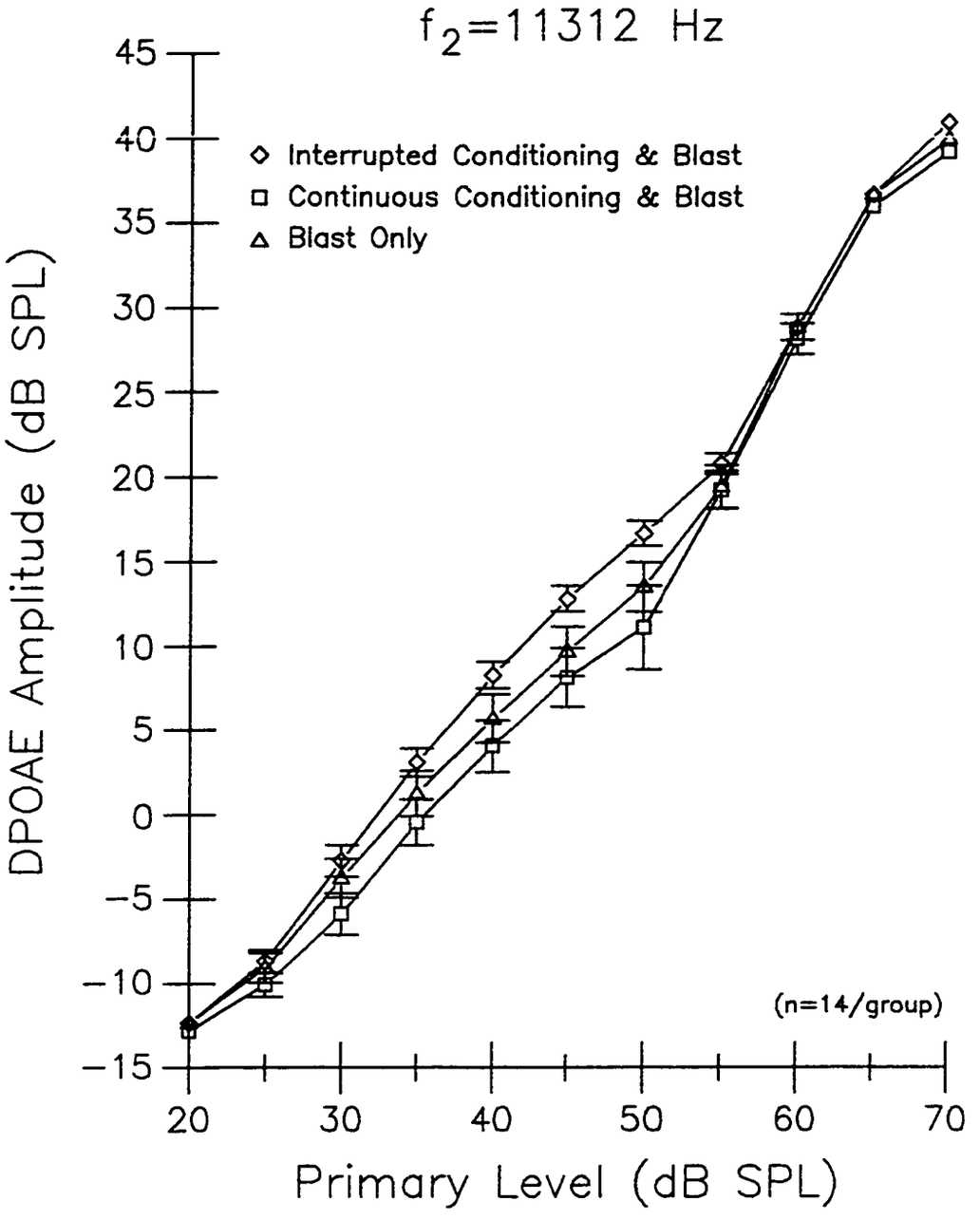


**Figure 3i.** The effect of the traumatizing exposure on DPOAE responses of unconditioned and sound conditioned animals at $f_2$ = 11312 Hz. For additional information, see legend for Figure 3a.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 5.** Three-way ANOVA Table - Analysis of the effects of the traumatizing noise exposure on the DPOAE responses of unconditioned and sound conditioned animals

| Source of Variation | DF | SS | MS | F | P |
|---|---|---|---|---|---|
| Group | 2 | 122.143 | 61.071 | 4.206 | 0.015 |
| Frequency | 8 | 174876.183 | 21859.523 | 1505.503 | <0.001 |
| Intensity | 10 | 544033.100 | 54403.310 | 3746.849 | <0.001 |
| Group x Frequency | 16 | 2422.114 | 151.382 | 10.426 | <0.001 |
| Group x Intensity | 20 | 360.915 | 18.046 | 1.243 | 0.208 |
| Frequency x Intensity | 80 | 64228.480 | 802.856 | 55.294 | <0.001 |
| Group x Frequency x Intensity | 160 | 2331.570 | 14.572 | 1.004 | 0.473 |
| Residual | 3861 | 56060.757 | 14.520 | | |
| Total | 4157 | 844435.262 | 203.136 | | |

**Table 6.** Summary of the Tukey multiple comparison test results for the main effect of Group found for DPOAE responses when pooling the data across Frequency and Intensity for the Blast Only (BLA), Continuous Conditioning then Blast (C&B), and Interrupted Conditioning then Blast (I&B) Groups.

| Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|
| I&B vs. C&B | 0.401 | 3 | 3.919 | Yes |
| I&B vs. BLA | 0.0931 | 3 | 0.910 | Yes |
| BLA vs. C&B | 0.308 | 3 | 3.009 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 7.** Summary of the Tukey multiple comparison test results for the Group x Frequency interaction found for DPOAE responses when pooling the data across Intensity for the Blast Only (BLA), Continuous Conditioning then Blast (C&B), and Interrupted Conditioning then Blast (I&B) Groups.

| Frequency | Comparison | Diff of Means | p | q | P<0.05 |
|---|---|---|---|---|---|
| 707 Hz | BLA vs. I&B | 1.534 | 3 | 4.997 | Yes |
| | BLA vs. C&B | 0.871 | 3 | 2.838 | Yes |
| | C&B vs. I&B | 0.663 | 3 | 2.159 | Yes |
| | | | | | |
| 1000 Hz | BLA vs. I&B | 2.121 | 3 | 6.908 | Yes |
| | BLA vs. C&B | 1.084 | 3 | 3.529 | Yes |
| | C&B vs. I&B | 1.037 | 3 | 3.379 | Yes |
| | | | | | |
| 8000 Hz | BLA vs. I&B | 4.887 | 3 | 8.312 | Yes |
| | BLA vs. C&B | 2.143 | 3 | 3.645 | Yes |
| | C&B vs. I&B | 2.744 | 3 | 4.667 | Yes |
| | | | | | |
| 11312 Hz | BLA vs. I&B | 5.148 | 3 | 8.756 | Yes |
| | BLA vs. C&B | 2.102 | 3 | 3.576 | Yes |
| | C&B vs. I&B | 3.046 | 3 | 5.180 | Yes |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CHAPTER 5

# DISCUSSION

Prior exposure to moderate-level acoustic stimulation (i.e., sound conditioning) has been shown to reduce (and in some instances prevent) the deleterious effects of subsequent higher level (and usually damaging) exposures (Canlon et al., 1988, 1992; Campo et al., 1991; Henderson et al., 1992; Ryan et al., 1994). Both continuous and interrupted schedules of moderate-level noise have been used as conditioning exposures and both have been effective in providing protection against subsequent noise trauma. However, there is evidence to suggest that (1) continuous noise exposures are more damaging to the cochlea than interrupted exposures of equal acoustic energy (Bohne et al., 1985, 1987; Fredelius and Wersäll, 1992), and (2) continuous and interrupted noise exposures differ in the pattern of auditory sensitivity change that they produce over time (i.e., asymptotic threshold shift vs. toughening; Carder and Miller, 1972; Miller et al., 1963). A question arises as to whether there are differences in the amount of protection afforded by prior conditioning of the auditory system with a moderate-level continuous or interrupted noise exposure schedule.

The purpose of this study was to test the hypothesis that differences exist in the amount of protection provided by prior sound conditioning with continuous versus interrupted, moderate-level noise. These differences were



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

determined by monitoring the changes that occurred in distortion product otoacoustic emission (DPOAE) amplitude growth functions after a subsequent higher level traumatizing exposure in guinea pigs (*Cavia cobaya*) conditioned with either continuous or interrupted noise. DPOAEs were chosen for study because they are believed to reflect the mechanical properties of the cochlea, particularly as related to the status of outer hair cell (OHC) function (Mountain, 1980; Siegel and Kim, 1982; Siegel et al., 1982). Both conditioning exposure schedules had the same total acoustic energy consistent with the Equal Energy Hypothesis (EEH; Eldred et al., 1955). This equal energy requirement was important in the design of the current experiment because it yielded noise exposures that (in theory) differed only in their temporal pattern.

The major results of this study demonstrating the effects of the sound conditioning exposures, the effects of the traumatizing noise exposure, and the effects of various combinations of the sound conditioning and traumatizing noise exposures on DPOAE amplitude growth functions are summarized below:

(1) The interrupted sound conditioning noise exposure was significantly less damaging to the cochlea than the continuous conditioning noise. This result does not support the validity of the EEH which assumes that the cumulative damage to the auditory system is a function of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the total acoustic energy received, regardless of the distribution of energy over time.

(2) Overall, there were significant differences between the groups of animals exposed to the traumatizing noise exposure (unconditioned vs. conditioned). Specifically, there was some amount of protection afforded by prior sound conditioning with the interrupted moderate-level noise exposure used in this study. However, the overall effect of the continuous sound conditioning protocol seemed to render the auditory system more susceptible to the traumatizing noise exposure when compared with the DPOAE responses of the unconditioned group.

(3) Sound conditioning with the interrupted, moderate-level noise prior to exposure to the traumatic noise produced a dual effect on the DPOAE responses depending upon the $f_2$ test frequency. The results revealed an apparent trend towards an increased susceptibility to the traumatizing noise exposure in the sound conditioned animals in the lower test frequency range ($f_2$ = 707-2000 Hz) and some degree of protection in the test frequency range spanning $f_2$ frequencies of 2828-11312 Hz.

**5.1 Baseline DPOAE responses**

A thorough examination of the DPOAE amplitude growth functions in aged normal guinea pigs was first performed to establish the baseline responses for the DPOAE parameters (e.g., $f_2/f_1$ ratio and $f_2$ test frequencies) used in this

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

study. The mean DPOAE amplitude growth functions obtained from the Aged Normal Group (Figure 2 (a-i), filled circles) were relatively consistent with the normative DPOAE results of other studies that used guinea pigs as experimental subjects (Brown, 1987; Brown and Gaskill, 1990). The DPOAE amplitudes were generally 30-50 dB SPL below the level of the primary tones at each of the intensity levels and each frequency tested. Although there were instances where the amplitude growth functions were highly nonmonotonic (e.g., $f_2$ = 707- and 1000 Hz), the overall growth rate of the distortion product amplitudes was approximately linear (i.e., a 1 dB increase in DPOAE amplitude for every 1 dB increase in primary level).

The variability of the amplitude growth functions across animals was small at each frequency tested, with standard deviations of usually less than 3 dB. However, there was a tendency for increased variability for the lower frequency DPOAEs ($f_2$ = 707-, 1000-, and 1414 Hz), especially in the highly nonmonotonic regions of the amplitude growth functions (primary tones ranging from 45 to 65 dB SPL). In such cases, the standard deviations were no more than 6.5 dB. When the frequency of $f_2$ was 2828-, 4000-, and 5656 Hz, an increase in intersubject variability also occurred in the region of the DPOAE amplitude growth functions generated by high-level primary tones (60-70 dB SPL). In this intensity region, the growth functions of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

many guinea pigs within this group exhibited rollover; however, the standard deviations still did not exceed 5 dB.

## 5.2 Effects of sound conditioning on DPOAE responses

### 5.2.1 Continuous sound conditioning

The animals subjected to the continuous sound conditioning protocol were exposed to an 89 dB SPL octave band noise (1.0-2.0 kHz) presented 24 hours per day for 11 consecutive days. The mean DPOAE amplitude growth functions obtained from the Continuous Conditioning Group are shown in Figure 2 (a-i; open down triangles). In order to better describe the effects of continuous sound conditioning on DPOAE responses, the differences in the amplitude growth functions between the Aged Normal Group (filled circles) and the Continuous Conditioning Group were obtained by subtracting the average DPOAE amplitudes of the sound conditioned group from the baseline DPOAE responses. The mean DPOAE amplitude differences between the two groups at each primary level and frequency are listed in Table 8. The shaded area of the table designates where statistically significant differences occurred between the groups as determined by the results of Tukey multiple comparisons tests ($P < 0.05$). Figure 4 provides a graphical representation of the mean amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero represent the magnitude of the amplitude reductions induced by the noise

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 8.** Mean amplitude difference data (in dB) between the Aged Normal Group and the Continuous Conditioning Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | -0.36 | 0.29 | 0.16 | 0.16 | -0.07 | 0.38 | 1.09 | 0.86 | 1.06 |
| 25 | -0.11 | 0.15 | 0.15 | -0.25 | 0.24 | 1.82 | 5.12 | 2.74 | 2.34 |
| 30 | 0.52 | 0.10 | 0.27 | 0.70 | 0.60 | 5.88 | 8.44 | 3.51 | 2.14 |
| 35 | 1.28 | 1.65 | 0.92 | 1.70 | 4.00 | 11.48 | 8.32 | 2.97 | 1.83 |
| 40 | 5.01 | 5.14 | 6.27 | 6.80 | 9.27 | 14.49 | 7.70 | 2.48 | 1.59 |
| 45 | 7.56 | 8.88 | 11.38 | 12.64 | 12.63 | 15.22 | 7.55 | 2.04 | 1.26 |
| 50 | 4.52 | 7.55 | 12.42 | 17.08 | 16.39 | 14.89 | 7.74 | 2.07 | 1.24 |
| 55 | 0.92 | -2.24 | 7.76 | 18.20 | 16.54 | 12.12 | 6.75 | 2.85 | 1.96 |
| 60 | 7.41 | -0.92 | 5.53 | 13.90 | 15.03 | 7.74 | 5.61 | 2.44 | 2.91 |
| 65 | 6.52 | 6.33 | 10.36 | 10.54 | 12.04 | 4.59 | 5.04 | 1.51 | 1.81 |
| 70 | 4.22 | 6.91 | 13.77 | 10.26 | 4.02 | -0.56 | 3.06 | 1.44 | 0.75 |

The shaded area represents statistically significant differences between the Aged Normal Group and the Continuous Conditioning Group ($P<0.05$).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

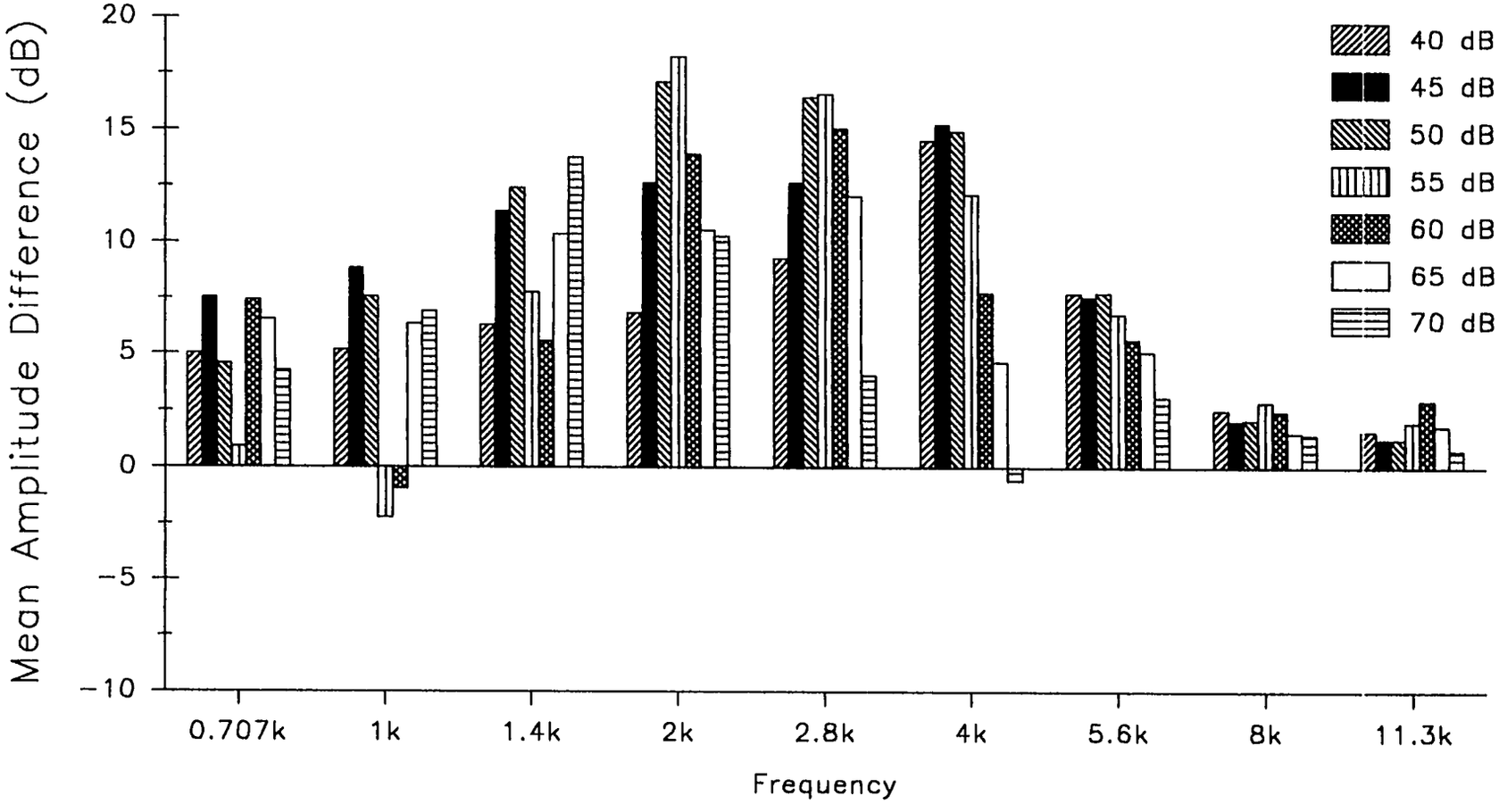


**Figure 4.** The effect of continuous sound conditioning on normal DPOAE responses. Data are presented as the mean amplitude differences between the Aged Normal Group and the Continuous Conditioning Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

exposure, whereas the negative excursions from zero show where the magnitude of the DPOAE responses were actually larger in the exposed group than in the unexposed controls.

The continuous conditioning exposure caused reductions in DPOAE amplitudes in a frequency- and intensity-dependent manner. The overall bell shape of Figure 4 demonstrates the frequency-dependence of the noise-induced effects on the DPOAE responses. The maximum effect of the noise exposure occurred in the mid-frequency range of the frequencies tested, while effects were not as great in the lower and higher frequencies. Specifically, the greatest amplitude reductions (approximately 12-18 dB) occurred in the frequency range spanning $f_2$ frequencies of 1414-4000 Hz. This frequency region corresponds to the center and upper cutoff frequency of the noise exposure band used in this study (octave band noise; 1.0-2.0 kHz), and extends to one octave above the upper cutoff frequency. This finding is not surprising, because it is consistent with previous reports showing that the maximum effect of an exposure can occur in the same frequency region of the exposure and/or approximately ½-1 octave above the upper cutoff frequency for bands of noise of reasonably constant spectrum level (Davis et al., 1943; Ward, 1976; Mitchell et al., 1977; Salvi et al., 1982). Smaller reductions (approximately 5-8 dB) were found at $f_2$ frequencies of 707-, 1000- and 5656 Hz, while at 8000- and 11312 Hz, the magnitude of the amplitude reductions was only 1-3 dB.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

The pattern of the individual bars plotted at each frequency illustrates the intensity-dependence of the noise-induced effects on the DPOAE responses. In most cases, the greatest decreases in amplitude occurred for primary levels ranging from 40-60 dB SPL. This result is consistent with the idea that DPOAEs elicited by low-to-moderate level primary tones are physiologically vulnerable to the oto-traumatic effects of noise exposure (Kim, 1980; Zurek et al., 1982; Subramaniam et al., 1994a,b). It is within this intensity range that the active, nonlinear processes of the OHCs normally exert their greatest influence. Puel et al. (1988a) speculated that it is the active process that is affected first during acoustic trauma. At the lower $f_2$ frequencies (707- and 1000 Hz), there were actually places within the amplitude growth functions where the responses of the sound conditioned group were better or not much different than those of the normal control group. This occurred for primary levels ranging from 50-60 dB SPL. It is within this intensity range where a large dip occurred in the amplitude growth functions of the unexposed group of animals.

The results of the present study demonstrating changes in DPOAE amplitude growth functions in guinea pigs after exposure to long-term continuous moderate-level noise differ from the findings of Canlon and Fransson (1995), who also tested the effects of continuous sound conditioning on DPOAEs in guinea pigs. These authors contend that their

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

continuous sound conditioning protocol (81 dB SPL, 1 kHz pure-tone presented continuously for 24 days) did not cause any significant alterations in $2f_1$-$f_2$ DPOAE amplitudes at frequencies of 1.75-, 2.1-, 2.8-, and 3.5 kHz. Five animals were tested before the sound conditioning exposure and then on days 1, 5, 10, 15, and 24 of the conditioning protocol. The results showed that there were changes (up to 10 dB) in the DPOAE amplitude growth functions during the initial stages of the sound conditioning protocol (days 1, 5, and 10) in some, but not all animals. However, by the end of the 24 day exposure, all animals had DPOAE responses similar to their pre-conditioned values.

Despite the fact that the continuous sound conditioning protocols used in the experiments mentioned above were dissimilar (i.e., 89 dB SPL octave band noise (1.0-2.0 kHz) for 11 days vs. 81 dB SPL, 1 kHz pure tone for 24 days), there are other differences in the experimental design of the Canlon and Fransson study (1995) that might possibly account for the lack of detection of significant DPOAE amplitude changes induced by their sound conditioning exposure. First, the same five guinea pigs were exposed and tested on various days (days 1, 5, 10, 15, and 24) throughout their continuous sound conditioning protocol (longitudinal study). However, within the manuscript, the length of time required for testing the DPOAE responses of each animal was never discussed. Included in this unknown time period would be (1) the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

amount of time for the animals to respond to the anesthesia, (2) the actual time required for DPOAE measurement, and (3) the amount of time needed for the animals to recover from the effects of the anesthesia before being placed back into the exposure booth. These periods of rest from the moderate-level stimulation may have influenced the DPOAE measures in a manner similar to that of an interrupted exposure (i.e., an initial reduction in DPOAE amplitudes over the initial days of the conditioning exposure followed by a return toward pre-exposure values as the exposure continues; Subramaniam et al., 1994a,b; 1995).

Secondly, it might be that the actual DPOAE frequencies chosen for study by Canlon and Fransson (1995) were not generated within the region along the cochlear partition that was affected by the 1 kHz pure tone conditioning exposure. Again, the region of DPOAE generation is thought to be near, or at, the $f_2$ place on the cochlear partition (Matthews and Molnar, 1986; Brown et al., 1992; Allen and Fahey, 1993; Puel et al., 1995). The lowest frequency DPOAE tested by Canlon and Fransson was $2f_1-f_2$ = 1.75 kHz ($f_2/f_1$=1.225; $f_1$=2.258 kHz, $f_2$=2.766 kHz). The frequency of $f_2$ in this case is approximately 1½ octaves above the frequency of the pure-tone, moderate-level conditioning exposure. This means that if the exposure was such that it caused only very localized changes in cochlear function in the region of the 1 kHz

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

conditioning tone, then it would be expected that DPOAEs with primary frequencies (especially $f_2$) outside of this region would be, for the most part, unaltered by the exposure. Recently, Skellett et al. (1996) showed frequency-dependent and very localized reductions in the $2f_1$-$f_2$ DPOAE amplitude growth functions of guinea pigs exposed continuously for 3 and 11 days to a noise with spectral characteristics similar to the one used in this study (1.1 - 2.0 kHz). The intensity level of this noise exposure, however, was only 65 dB SPL. These reductions occurred only when the frequency of $f_2$ was within the noise exposure band.

In support of the findings of the present study, other investigators have also shown changes in their response measurements immediately after the final day of a continuous sound conditioning protocol. However, in the studies performed by Ryan et al. (1994) and Fowler et al. (1995), auditory brainstem response thresholds were measured after the final day of a long-term, moderate-level noise exposure. Ryan et al. (1994) reported threshold shifts of 0-40 dB (depending upon the test frequency) from their pre-exposure values in Mongolian gerbils immediately following a three week exposure to an 81 dB SPL two-octave band noise (1414-5656 Hz). The greatest threshold shifts (approximately 40 dB) were measured for test frequencies of 4- and 8 kHz, one which is within the noise exposure band (4 kHz) and the other which is ½ octave above the upper

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

cutoff frequency of the noise band (8 kHz). Smaller shifts occurred for test frequencies 0.5-, 1-, and 2 kHz -- approximately 10-, 10-, and 20 dB, respectively. The auditory brainstem response threshold at 16 kHz was virtually unaffected. This pattern of threshold shift caused by sound conditioning is similar to the pattern of DPOAE amplitude growth function alterations measured in the present study (Figure 4), i.e., the maximal effect of the continuous noise exposure occurred at test frequencies within and slightly above the noise exposure band.

Fowler et al. (1995) also demonstrated frequency-specific increases in the auditory brainstem response thresholds of CBA/Ca mice for several different continuous sound conditioning protocols. Three groups of mice were continuously exposed to a narrowband noise centered at 4.5 kHz presented at several different intensities and durations. When the noise was presented at a level of 86 dB SPL for 10 days, the threshold shifts measured on the last day of the conditioning protocol in the first group of mice were approximately 20 dB at test frequencies of 4- and 6.3 kHz, and 10- and 6 dB at test frequencies of 8- and 10 kHz. No significant threshold shifts occurred at 12.5- and 16 kHz. When the level of the noise was reduced to 80 dB SPL and the exposure duration was again 10 consecutive days, the threshold shifts obtained from a second group of mice were limited to the two lowest test frequencies. The mean threshold shifts at 4- and 6.3 kHz were approximately

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

25- and 14 dB, respectively. A third group of mice was exposed to the noise at a level of 80 dB SPL; however, for this group the duration of the exposure was increased to 24 days. Under these conditions, there were threshold shifts across all of the test frequencies. Statistical significance was reached at 4-, 6.3-, 8-, and 12.5 kHz. Still, the largest threshold shift occurred near the center frequency of the noise band at the test frequency of 4 kHz. The magnitude of this shift was approximately 22 dB. Threshold shifts of 12-15 dB were measured at 6.3-, 8-, and 12.5 kHz. While there was no statistical significance at 10- and 16 kHz, there was an increase in threshold of 6- and 10 dB, respectively. Thus, by altering the duration and/or intensity level of the noise exposure, Fowler et al. (1995) showed that the frequency region affected by the conditioning noise could be altered. However, more important is the fact that a similar pattern of threshold shift was caused by the continuous sound conditioning protocol used by these investigators as was found in the DPOAE amplitude growth function alterations measured in the present study (Figure 4). Again, the maximal effect of the continuous noise exposure occurred at test frequencies within and slightly above the noise exposure band, with lesser effects outside of this frequency region.

Fowler et al. (1995) exposed a fourth group of mice to a 75 dB SPL, 1 kHz pure tone continuously for 10 days. This exposure was selected as an extrapolation of the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

guinea pig continuous conditioning paradigm used by Canlon et al. (1988) and Canlon and Fransson (1995). The auditory brainstem response thresholds taken immediately upon removal from the conditioning tone revealed no significant threshold shifts for the frequencies tested (4-, 6.3-, 8-, 10-, 12.5-, and 16 kHz). The lack of any measurable threshold shift across the test frequencies in response to the pure tone exposure was similar to the findings reported by Canlon et al. (1988) and Canlon and Fransson (1995). However, as mentioned earlier, if the exposure was such that it caused only very localized changes in cochlear function in the region of the 1 kHz conditioning tone, then it would be expected that frequency regions two octaves and above this region would be, for the most part, unaltered by the exposure and the response measurements unaffected.

Thus, the frequency-specific changes in the DPOAE response measurements caused by the continuous sound conditioning protocol used in this study are supported by other evidence in the literature (Ryan et al., 1994; Fowler et al., 1995). When the response measurements (either the $f_2$ frequencies when measuring DPOAEs or the test frequencies used to elicit an auditory brainstem response) were within the frequency region of the noise band or slightly above it, reductions in the DPOAE amplitudes or increases in the auditory brainstem response thresholds occurred.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

### 5.2.2 Interrupted sound conditioning

The animals subjected to the interrupted sound conditioning protocol were exposed to a 95 dB SPL octave band noise (1.0-2.0 kHz) presented 6 hours per day for 11 consecutive days. The mean DPOAE amplitude growth functions obtained from the Interrupted Conditioning Group are shown in Figure 2 (a-i; open circles). In order to better describe the effects of interrupted sound conditioning on DPOAE responses, the differences in the amplitude growth functions between the Aged Normal Group and the Interrupted Conditioning Group were obtained by subtracting the average DPOAE amplitudes of the sound conditioned group from the baseline DPOAE responses. The mean DPOAE amplitude differences between the two groups at each primary level and frequency are listed in Table 9. The shaded area of the table designates where statistically significant differences occurred between the groups as determined by the results of Tukey multiple comparisons tests ($P < 0.05$). Figure 5 provides a graphical representation of the mean differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero represent the magnitude of the amplitude reductions induced by the noise exposure, whereas the negative excursions from zero show where the magnitude of the DPOAE responses were actually larger in the exposed group than in the unexposed controls.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 9.** Mean amplitude difference data (in dB) between the Aged Normal Group and the Interrupted Conditioning Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | -0.34 | -0.26 | -0.22 | -0.54 | -0.25 | 0.25 | 0.28 | -0.66 | -0.04 |
| 25 | -0.10 | -0.36 | -0.44 | -0.43 | -0.41 | 1.10 | 2.32 | -1.29 | 0.10 |
| 30 | 0.24 | -0.39 | -0.40 | 0.14 | 0.50 | 5.50 | 4.32 | -1.21 | 0.06 |
| 35 | 0.44 | 0.40 | 1.00 | 1.22 | 3.35 | 11.31 | 5.60 | -0.96 | -0.16 |
| 40 | 0.73 | 2.02 | 5.01 | 6.53 | 8.09 | 15.01 | 6.37 | -0.65 | -0.27 |
| 45 | 0.29 | 1.75 | 7.76 | 11.28 | 10.90 | 16.60 | 5.94 | -0.46 | -0.16 |
| 50 | -2.86 | -1.80 | 5.89 | 13.59 | 12.97 | 14.19 | 5.65 | 0.01 | -0.06 |
| 55 | -6.52 | -9.38 | 2.10 | 11.23 | 12.65 | 10.23 | 5.34 | 1.17 | 1.38 |
| 60 | 2.47 | -5.06 | 2.12 | 8.34 | 13.20 | 8.10 | 3.96 | 0.96 | 1.87 |
| 65 | 5.35 | 5.26 | 7.48 | 7.88 | 13.17 | 4.78 | 2.82 | 0.10 | 1.27 |
| 70 | 5.61 | 8.14 | 7.06 | 8.83 | 8.11 | 0.61 | 2.58 | 0.04 | 0.10 |

The shaded area represents statistically significant differences between the Aged Normal Group and the Interrupted Conditioning Group ($P<0.05$).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

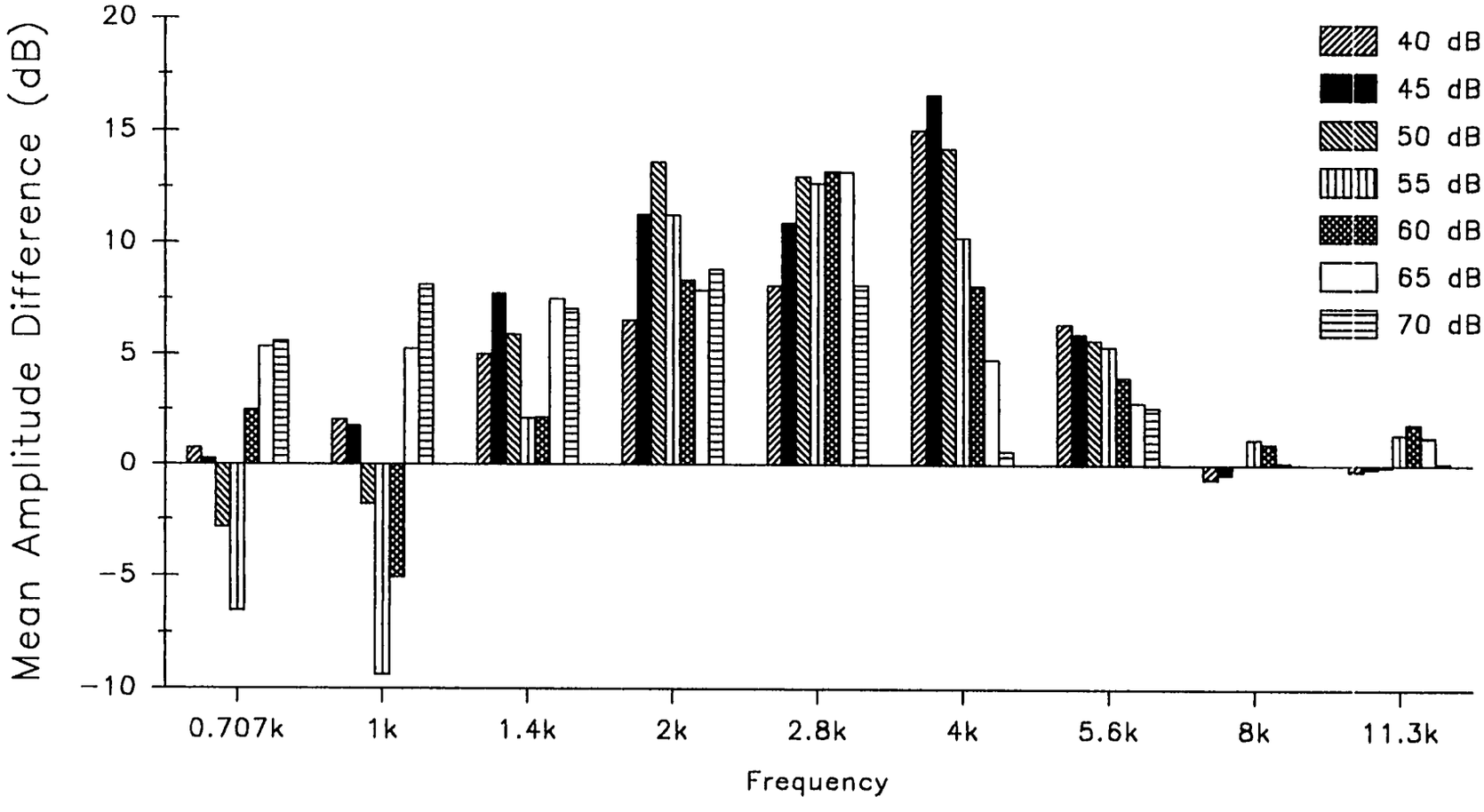


**Figure 5.** The effect of interrupted sound conditioning on normal DPOAE responses. Data are presented as the mean amplitude differences between the Aged Normal Group and the Interrupted Conditioning Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

The interrupted conditioning exposure also caused reductions in DPOAE amplitudes in a frequency- and intensity-dependent manner. The overall "quasi" bell-shaped pattern of Figure 5 demonstrates the frequency-dependence of the noise-induced effects on the DPOAE responses. The maximum effect of the noise exposure occurred in the mid-frequency range of the frequencies tested, while effects were not as great in the lower and virtually non-existent in the higher frequencies. For this exposure protocol however, the greatest amplitude reductions occurred in a narrower frequency range (relative to the continuous sound conditioning protocol), spanning $f_2$ frequencies of 2000-4000 Hz. The magnitude of the reductions within this range was approximately 11-16 dB. This frequency region corresponds to the upper cutoff frequency of the noise exposure band used in this study (octave band noise; 1.0-2.0 kHz) and extends to one octave above the upper cutoff frequency.

The pattern of the individual bars plotted at each $f_2$ frequency illustrates the intensity-dependence of the noise-induced effects on the DPOAE responses. In the frequency region where the interrupted noise exposure had its greatest effect ($f_2$ = 2000-4000 Hz), the largest decreases in amplitude occurred for primary levels ranging from about 40-60 dB SPL. This result is consistent with the idea that DPOAEs elicited by low-to-moderate level primary tones are physiologically vulnerable to the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

oto-traumatic effects of noise exposure (Kim, 1980; Zurek et al., 1982; Subramaniam et al., 1994a,b). It is within this intensity range that the active, nonlinear processes of the OHCs normally exert their greatest influence.

At the lower $f_2$ frequencies (707- and 1000 Hz), there were actually intensity levels of the amplitude growth functions where the DPOAEs amplitudes recorded for the sound conditioned group were larger than those of the normal control group. These $f_2$ frequencies coincide with the lower cutoff frequency of the noise exposure band (1000 Hz) and a frequency ½ octave below it (707 Hz). These elevations in the DPOAE amplitudes relative to the normal controls occurred for primary levels ranging from 50-60 dB SPL. It is within this intensity range where a large dip occurred in the amplitude growth functions of the unexposed group of animals.

The increased amplitudes found within the DPOAEs of the sound conditioned animals at frequencies bordering the noise exposure band are consistent with the results of Boettcher and Schmiedt (1995). These investigators reported elevated DPOAE amplitudes in Mongolian gerbils exposed to an 80 dB SPL octave band noise centered at 4 kHz on an interrupted schedule for either 1 or 12 days. Similarly, the amplitude elevations occurred for primary levels of 50 and 60 dB SPL when DPOAEs whose $f_2$ frequencies were close to the lower cutoff frequency of their noise exposure band ($\leq$ 2.8 kHz) were measured. However, since

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

these authors did not show the average DPOAE amplitude growth functions of their unexposed animals, nor did they mention the existence of a nonmonotonic dip in this intensity region of these normal amplitude growth functions, it is not known if the noise exposures used in each study had similar effects overall.

Further, when studying the effects of noise-induced hearing loss on DPOAEs in humans, Kim et al. (1992) obtained similar results. These investigators found that that DPOAE amplitudes were larger than normal at the edge of a hearing loss in subjects who exhibited audiograms that were typical of those obtained when there was prior history of noise exposure. This type of audiogram is characterized by a "notch" (elevated thresholds) at 4 kHz with normal sensitivity at lower frequencies (2 kHz and below). In these subjects, DPOAE amplitudes were approximately 10-15 dB higher in the frequency region between 1- and 2 kHz when compared to the responses of normal hearing subjects. While not conclusive, the results of all three studies suggest that the elevated DPOAE amplitudes measured in the frequency region bordering a noise-induced cochlear lesion, may be related to the effects of noise exposure on the mechanism(s) responsible for DPOAE generation.

Other researchers have also studied the effects of interrupted sound conditioning protocols on DPOAEs. Subramaniam et al. (1994a,b; 1995) examined the changes in DPOAE amplitude growth functions of chinchillas in response

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

to both low- and high-frequency interrupted sound conditioning protocols. The studies by Subramaniam and colleagues, however, were longitudinal in nature in that they tracked the responses of a small number of animals over the course of the conditioning exposure. To compare the results found in the present experiment to those reported by Subramaniam et al. (1994 a,b; 1995), focus was placed on the DPOAE responses measured immediately after the final day of the interrupted conditioning exposure.

The low frequency exposure used by Subramaniam et al. (1994a) was a 95 dB SPL octave band noise centered at 0.5 kHz presented twice a day for 15 days using a 3 hours "on"/9 hours "off" schedule. DPOAEs amplitude growth functions were measured in five chinchillas (n=10 ears) at the geometric mean frequencies of 1, 2, 3, 4, 6, and 8 kHz on various days during the sound conditioning protocol. DPOAE amplitudes decreased significantly during the first few days of the interrupted noise exposure and then began to recover towards baseline as the exposure duration continued. By the final day of the noise exposure (day 15), there were residual losses at all frequencies tested. Oddly, the losses were smaller for frequencies closer to the noise exposure band (e.g., 1- and 2 kHz) and greater for frequencies farther removed (e.g., 8 kHz).

In a similar study, Subramaniam et al. (1994b) exposed six chinchillas to a conditioning noise of the same intensity and spectral characteristics as in the study

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

mentioned above; however the exposure was repeated over 10 consecutive days on a 6 hours "on"/18 hours "off" schedule. DPOAEs amplitude growth functions were measured at the geometric mean frequencies of 1-, 2-, 4-, and 8 kHz on various days during the sound conditioning protocol (days 2, 4, 6, 8, and 10). Results showed that the changes in DPOAE amplitudes were frequency dependent. Specifically, at 1- and 2 kHz, the average DPOAE responses decreased significantly by the first few days of the exposure protocol, but recovered to within 10 dB of the pre-exposure values by the tenth and final day of exposure. At 4 kHz, very little recovery of the DPOAE amplitudes was found and no recovery was reported for the 8 kHz amplitude growth functions.

The pattern of the DPOAE amplitude reductions measured in the present experiment was different from the results of both of the Subramaniam et al. (1994 a,b) studies discussed above. The results of the present study showed a relatively predictable pattern of DPOAE loss in that the maximum loss was confined to the frequency region very near the frequency band of the noise exposure. Again, this region corresponded to the upper cutoff frequency of the noise exposure band used in this study (octave band noise; 1.0-2.0 kHz) and extended to one octave above the upper cutoff frequency. Small reductions in DPOAE amplitudes were found outside of this region, especially in the higher frequencies tested. This same pattern of damage was not

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

reported by Subramaniam et al. (1994a,b). Although the noise used by Subramaniam et al. was a low frequency noise (octave band noise centered at 0.5 kHz), there were substantial reductions in the DPOAE amplitudes even at high frequencies, i.e. 4 and 8 kHz. This spread of cochlear damage in response to low frequency noise exposure has been previously observed (Zurek et al., 1982; Clark et al.,1987; Subramaniam et al., 1991a).

Subramaniam et al. (1995) also examined the changes in DPOAE amplitude growth functions of chinchillas in response to a high frequency, interrupted sound conditioning protocol. Five animals were exposed to an 85 dB SPL octave band noise centered at 4 kHz for 10 consecutive days on a 6 hours "on"/18 hours "off" schedule. DPOAE amplitude growth functions were measured for $f_1$ frequencies set at 1-, 2-, 3-, 4-, 5.6-, and 8 kHz with an $f_2/f_1$ ratio of 1.2. They found that initially, there was a substantial decrease in DPOAE amplitudes followed by either a partial or a complete return to pre-exposure values depending upon the test frequency. At 3 kHz, the recovery towards baseline was complete by day 10 of the exposure. At 8 kHz, recovery was almost complete with DPOAE amplitudes within 5 dB of the pre-exposure measurements. However, for DPOAEs measured when the $f_1$ frequencies were 4.0 and 5.6 kHz, the amplitudes were 9-12 dB lower than the pre-exposure amplitudes. These results were similar to the changes observed in the DPOAE amplitude growth functions of the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

present experiment in that by the final day of the interrupted exposure, the reductions in the DPOAE amplitudes were fairly localized to frequencies within the noise exposure band.

### 5.2.3 Comparison of the effects of the two sound conditioning protocols - Testing the validity of the EEH

Although the two sound conditioning protocols used in the present experiment had equal acoustic energy, the resultant changes in DPOAE amplitude growth functions measured in the groups of guinea pigs exposed to either continuous or interrupted noise were not equivalent. Figures 4 and 5 show the mean DPOAE amplitude differences between the Continuous Conditioning Group and the Aged Normal Group, and the Interrupted Conditioning Group and the Aged Normal Group, respectively. When comparing these figures, it becomes apparent that overall, the interrupted conditioning noise was significantly less damaging to the cochlea than the continuous conditioning noise. Not only were the magnitudes of the noise-induced DPOAE amplitude reductions less in the animals conditioned with the interrupted noise as opposed to the continuous noise, but the range of $f_2$ frequencies affected by the interrupted exposure was also decreased. Therefore, these results do not support the validity of the EEH which assumes that the cumulative damage to the auditory system is a function of the <u>total</u> acoustic energy received, regardless of the distribution of energy over time (Eldred et al., 1955). This finding is backed by previous histological data

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

showing that while the pattern of hair cell damage was the same for a continuous vs. an interrupted noise exposure (both with equal acoustic energy), the magnitude of hair cell damage induced by the exposures was less for the interrupted exposure (Bohne et al., 1985, 1987; Fredelius and Wersäll, 1992). Thus, it is quite possible that the rest (quiet) periods within the interrupted exposure acted to minimize noise-induced hair cell damage and were responsible for the significantly smaller reductions in the DPOAE amplitudes (when compared to the continuous exposure) observed in this study.

As discussed earlier, both schedules of sound conditioning noise had their greatest overall effect in the mid-frequency range of the $f_2$ frequencies tested. This frequency region includes the center and upper cutoff frequencies of the noise exposure band used in this study (octave band noise; 1.0-2.0 kHz) and extends to one octave above the upper cutoff frequency. For the continuous conditioning noise, this range spanned from 1414-4000 Hz. Within this range, the peak effect occurred at 2000 Hz (the upper cutoff frequency of the noise exposure band), with maximum DPOAE amplitude reductions of 13-18 dB when the intensity of the primary tones was 45-60 dB SPL. For the interrupted conditioning noise, a narrower range of $f_2$ frequencies was maximally affected by the conditioning noise exposure, i.e., 2000-4000 Hz. In this case, the peak noise-induced effect occurred at 4000 Hz (one octave above

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the upper cutoff frequency of the noise exposure band), with maximum DPOAE amplitude reductions of 11-16 dB when the intensity of the primary tones was 40-55 dB SPL.

The reason for this upward shift in the frequency of maximum effect could possibly be related to the higher intensity level of the interrupted noise exposure. While the periods of rest within the interrupted noise serve to lessen the overall noise-induced effects on the DPOAE amplitude growth functions, the intensity level of the exposure may determine where (in terms of frequency) the maximum noise-induced changes occur. It appears that the lower the intensity of the exposure, the more localized are the changes in the response measurements to the frequency region of the noise exposure. With an increase in exposure level, there is an overall spread in the noise-induced reductions in the DPOAE amplitudes, with a shift in the maximum effect to higher frequencies outside of the noise exposure band.

An interesting result was found when comparing the effects of both schedules of conditioning noise on the DPOAE amplitude growth function at $f_2$ frequencies of 707- and 1000 Hz. In the average DPOAE responses of the Aged Normal Group, there are highly nonmonotonic regions of the amplitude growth functions (primary tone levels ranging from 50 to 60 dB SPL) at these frequencies. Different mechanisms have been suggested as the contributing factors to the dip that occurs in the amplitude growth functions of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

these low frequency DPOAEs: (1) phase cancellation between multiple acoustic components (Zwicker, 1986; Brown, 1987) and (2) the existence of two distortion product sources or generation sites, one which functions at low primary tone levels and requires the operation of active nonlinear cochlear processes, and another which functions at high primary tone levels and involves passive cochlear mechanisms (Rosowski et al., 1984; Brown, 1987; Norton and Rubel, 1990; Whitehead et al., 1992a,b). Both the continuous and interrupted conditioning exposures eliminated the nonmonotonic region from within the DPOAE amplitude growth functions at $f_2$ frequencies of 707- and 1000 Hz; however, the effects that each exposure had were quite different. The continuous conditioning noise, for the most part, induced an overall decrease in the amplitudes at each intensity level of the growth functions to below that of the normal response, and in doing so eliminated the nonmonotonic dips from the amplitude growth functions. This type of response is typical of noise-induced effects on DPOAEs. The interrupted conditioning noise, on the other hand, enhanced the DPOAE amplitudes within the intensity region of the curves where these dips existed (primary tone levels ranging from 50 to 60 dB SPL), so that the magnitude of the responses were actually larger than that of the normal response. It is possible that the interrupted noise exposure, in some way, altered the mechanism(s) responsible for generating such

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

nonmonotonicities. These alterations may have eliminated phase cancellations between multiple acoustic components that are thought to be responsible for generating the nonmonotonic dips found in the normal DPOAE amplitude growth functions of this low frequency region (Zwicker, 1986; Brown, 1987).

### 5.3 Effects of the traumatizing noise exposure on DPOAE responses

#### 5.3.1 Unconditioned animals (Blast Only Group)

The unconditioned animals of the Blast Only Group were housed at the animal care facility for 7-8 weeks and then exposed to a 105 dB SPL octave band noise (1.0-2.0 kHz) presented continuously for 3 consecutive days. DPOAE amplitude growth functions were measured 4 weeks after removal from the traumatizing noise exposure. The mean DPOAE amplitude growth functions obtained from the Blast Only Group are shown in Figure 3 (a-i; open up-triangles).

To show the effects of the traumatizing noise exposure on normal DPOAE responses, the differences in the amplitude growth functions between the Aged Normal Group and the Blast Only Group were obtained by subtracting the average DPOAE amplitudes of the group exposed to the traumatizing noise from the baseline DPOAE responses. The mean DPOAE amplitude differences between the two groups at each primary level and frequency are listed in Table 10. Figure 6 provides a graphical representation of the mean amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 10.** Mean amplitude difference data (in dB) between the Aged Normal Group and the Blast Only Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | -0.16 | 0.37 | -0.05 | -0.25 | -0.39 | -0.35 | 0.65 | 1.12 | 0.56 |
| 25 | -0.29 | 0.22 | -0.26 | -0.81 | -0.03 | 0.96 | 4.26 | 4.88 | 1.79 |
| 30 | 0.59 | -0.16 | -0.03 | 0.47 | 0.89 | 5.06 | 10.66 | 10.40 | 2.59 |
| 35 | 1.34 | 0.99 | 0.95 | 1.14 | 3.44 | 11.17 | 16.42 | 14.30 | 3.42 |
| 40 | 4.39 | 4.72 | 5.99 | 5.94 | 9.08 | 15.18 | 20.48 | 16.43 | 4.05 |
| 45 | 6.39 | 8.97 | 10.12 | 12.07 | 12.00 | 17.26 | 19.79 | 16.70 | 4.49 |
| 50 | 3.07 | 9.59 | 11.22 | 14.60 | 15.28 | 18.07 | 16.88 | 17.20 | 4.48 |
| 55 | -1.82 | 2.08 | 6.85 | 13.42 | 16.12 | 18.13 | 14.01 | 13.46 | 2.68 |
| 60 | 2.65 | 4.28 | 6.83 | 11.29 | 17.78 | 19.81 | 13.95 | 11.13 | 1.18 |
| 65 | 6.22 | 11.48 | 12.63 | 12.14 | 20.64 | 16.08 | 12.36 | 8.81 | 1.23 |
| 70 | 12.22 | 10.90 | 12.70 | 15.43 | 17.50 | 7.23 | 2.80 | 4.65 | 1.50 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

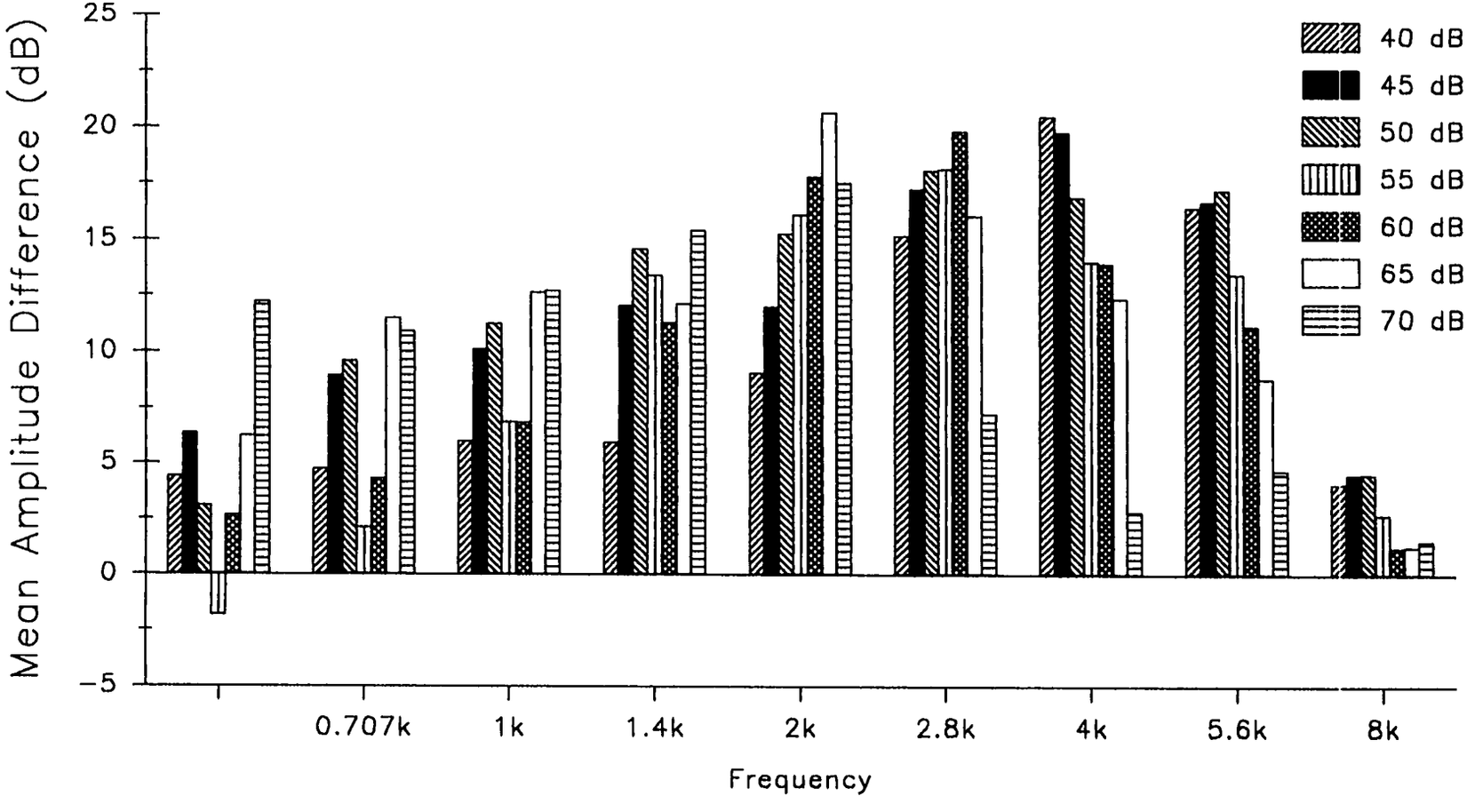


**Figure 6.** The effect of the traumatizing noise on normal DPOAE responses. Data are presented as the mean amplitude differences between the Aged Normal Group and the Blast Only Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

intensity levels (40-70 dB SPL). The positive excursions from zero represent the magnitude of the amplitude reductions induced by the noise exposure, whereas the negative excursions from zero show where the magnitude of the DPOAE responses were actually larger in the exposed group than in the unexposed controls.

The overall shape of Figure 6 demonstrates the frequency-dependence of the noise-induced effects on the DPOAE responses caused by the high-level, traumatizing exposure. This pattern was different than the patterns of the noise-induced effects obtained from groups of animals exposed only to the sound conditioning noise (Figures 4 and 5). The alterations in the DPOAE amplitude growth functions caused by this exposure were more widespread. The noise-induced reductions in DPOAE amplitudes were not only larger, but were also distributed across the entire test frequency range. The region of maximal effect was skewed toward the higher frequencies of $f_2$ tested. This region covered $f_2$ frequencies ranging from 2828-8000 Hz. The magnitudes of the DPOAE amplitude reductions within this frequency range were approximately 12-21 dB. Smaller reductions occurred for the lower frequencies of $f_2$ (707-2000 Hz). Still, the amplitude reductions within this low frequency range were quite large, with losses ranging from approximately 5-15 dB at intensity levels of the amplitude growth functions where the effects of the noise were maximal. The traumatizing noise had its least effect at

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the highest frequency of $f_2$ tested (f2=11312 Hz), with reductions of only 2-4 dB.

The pattern of the individual bars plotted at each frequency illustrates the intensity-dependence of the noise-induced effects on the DPOAE responses. In the frequency region where the traumatic noise exposure had its greatest effect, the largest decreases in amplitude occurred for primary levels ranging from about 40-60 dB SPL. For the DPOAE amplitude growth functions measured at $f_2$ frequencies of 707-2828 Hz, the largest amplitude reductions occurred for the high level primary tones tested (65-70 dB SPL), suggesting that this high intensity noise also affected passive cochlear mechanics within this frequency range. At the lower $f_2$ frequencies (707- and 1000 Hz), there were actually intensity levels of the amplitude growth functions where the responses of the sound conditioned group were better or not much different than those of the normal control group. This occurred for primary levels ranging from 50-60 dB SPL. It is within this intensity range where a large dip occurred in the amplitude growth functions of the unexposed group of animals.

### 5.3.2 Sound Conditioned animals

#### 5.3.2.1 Continuous sound conditioning

The animals in this group were exposed continuously for 11 days to an 89 dB SPL octave band noise (1-2 kHz), given 1 week to recover, and then exposed continuously to

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the 105 dB SPL traumatizing noise for 3 days. DPOAE amplitude growth functions were measured 4 weeks after removal from the traumatizing noise exposure. The mean DPOAE amplitude growth functions obtained from the Continuous Conditioning then Blast Group are shown in Figure 3 (a-i; open squares). To show the effects of the continuous conditioning/traumatizing noise exposure combination on normal DPOAE responses, the differences in the amplitude growth functions between the Aged Normal Group and the Continuous Conditioning then Blast Group were obtained by subtracting the average DPOAE amplitudes of the noise exposed group from the baseline DPOAE responses. The mean DPOAE amplitude differences between the two groups at each primary level and frequency are listed in Table 11. Figure 7 provides a graphical representation of the mean amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero represent the magnitude of the amplitude reductions induced by the noise exposure, whereas the negative excursions from zero show where the magnitude of the DPOAE responses were actually larger in the exposed group than in the unexposed controls.

The overall shape of Figure 7 demonstrates the frequency-dependence of the noise-induced effects on the DPOAE responses. This pattern of change caused by the traumatizing noise exposure in animals previously sound

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 11.** Mean amplitude difference data (in dB) between the Aged Normal Group and the Continuous Conditioning then Blast Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | -0.26 | -0.18 | -0.37 | -0.22 | -0.44 | -0.58 | 0.40 | 1.21 | 1.03 |
| 25 | -0.38 | -0.24 | -0.52 | -0.72 | -0.38 | 0.81 | 4.83 | 4.40 | 2.79 |
| 30 | -0.10 | -0.44 | -0.25 | -0.34 | 0.79 | 4.50 | 10.82 | 9.46 | 4.71 |
| 35 | 0.84 | 0.99 | 0.44 | 1.06 | 3.37 | 11.01 | 16.27 | 12.70 | 5.12 |
| 40 | 4.24 | 4.81 | 5.17 | 5.92 | 8.51 | 15.11 | 19.78 | 14.93 | 5.69 |
| 45 | 6.62 | 8.90 | 10.54 | 11.81 | 11.91 | 17.80 | 19.04 | 15.82 | 6.02 |
| 50 | 3.22 | 9.21 | 11.33 | 14.85 | 15.51 | 18.02 | 16.28 | 13.91 | 6.87 |
| 55 | -1.88 | 2.09 | 8.91 | 15.69 | 17.71 | 18.68 | 14.20 | 11.30 | 2.87 |
| 60 | 4.01 | 4.29 | 9.98 | 14.47 | 19.66 | 20.05 | 14.00 | 11.01 | 1.88 |
| 65 | 10.49 | 11.68 | 15.17 | 15.96 | 19.37 | 17.23 | 12.10 | 9.16 | 1.92 |
| 70 | 17.41 | 12.34 | 15.81 | 18.88 | 12.25 | 8.95 | 2.09 | 5.24 | 2.24 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

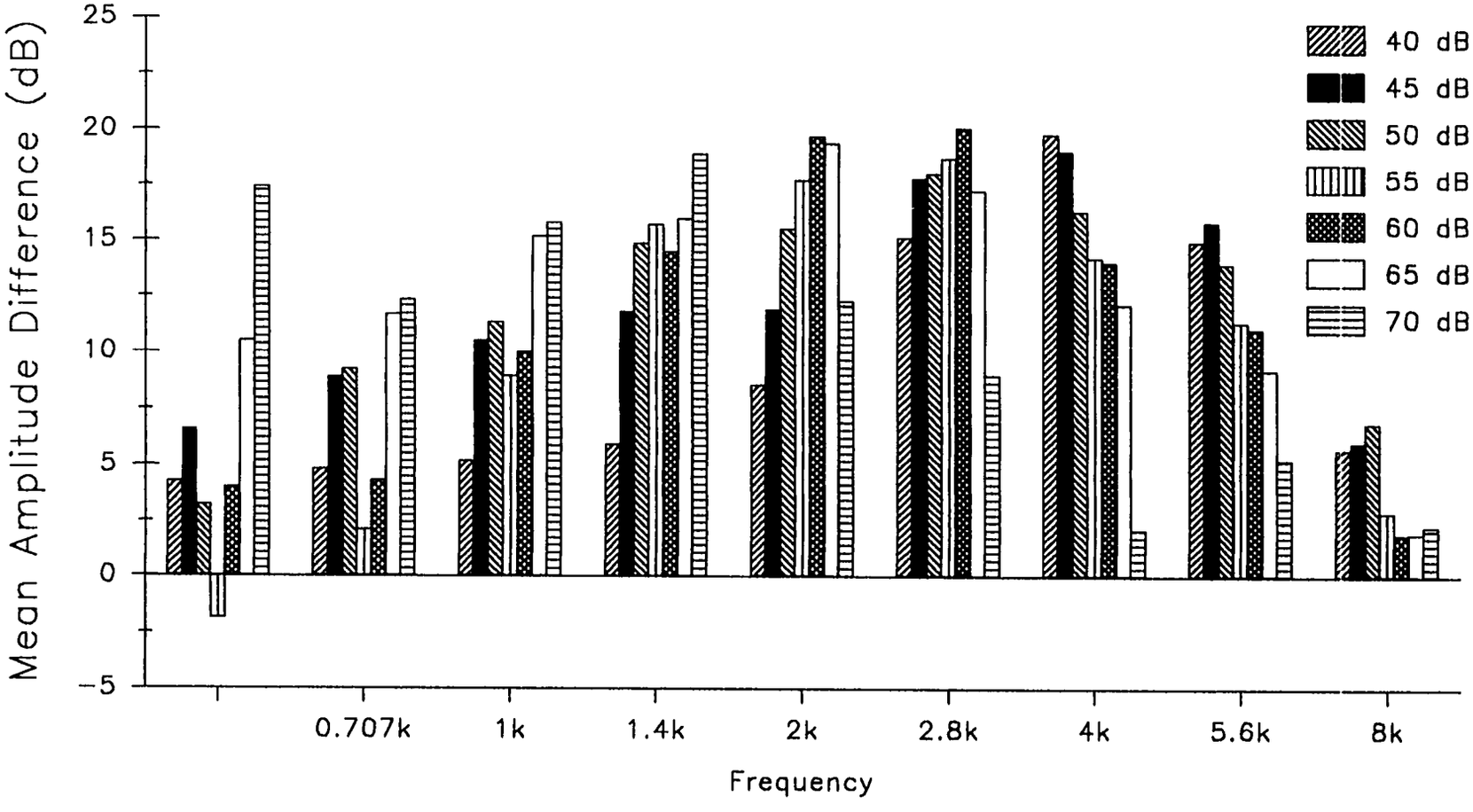


**Figure 7.** The effect of the continuous conditioning/traumatizing noise exposure combination on normal DPOAE responses. Data are presented as the mean amplitude differences between the Aged Normal Group and the Continuous Conditioning then Blast Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

conditioned on a continuous schedule is similar to that obtained for the unconditioned animals (Figure 6). Although similar, there were differences in the DPOAE responses between the unconditioned (Blast Only) group and the sound conditioned (Continuous Conditioning then Blast) group. These differences are discussed in detail in Section 5.3.3.1 as they relate to the possible protective role of the sound conditioning exposure.

**5.3.2.2 Interrupted sound conditioning**

The animals in this group were exposed 6 hours per day for 11 days to a 95 dB SPL octave band noise (1-2 kHz; 6 hours "on"/18 hours "off"), given 1 week to recover, then exposed continuously to the 105 dB SPL traumatizing noise for 3 days. DPOAE amplitude growth functions were measured 4 weeks after removal from the traumatizing noise exposure. The mean DPOAE amplitude growth functions obtained from the Interrupted Conditioning then Blast Group are shown in Figure 3 (a-i; open diamonds). To show the effects of the interrupted conditioning/traumatizing noise exposure combination on normal DPOAE responses, the differences in the amplitude growth functions between the Aged Normal Group and the Interrupted Conditioning then Blast Group were obtained by subtracting the average DPOAE amplitudes of the noise exposed group from the baseline DPOAE responses. The mean DPOAE amplitude differences between the two groups at each primary level and frequency are listed in Table 12. Figure 8 provides a graphical

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 12.** Mean amplitude difference data (in dB) between the Aged Normal Group and the Interrupted Conditioning then Blast Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | 0.11 | 0.04 | 0.27 | 0.22 | -0.19 | 0.26 | 0.87 | 1.02 | 0.54 |
| 25 | -0.05 | 0.09 | 0.04 | -0.01 | 0.09 | 1.64 | 5.06 | 4.21 | 1.42 |
| 30 | 0.48 | -0.15 | 0.12 | 0.59 | 0.67 | 5.37 | 11.38 | 8.64 | 1.56 |
| 35 | 1.31 | 0.93 | 1.18 | 1.68 | 3.54 | 11.11 | 17.06 | 11.50 | 1.56 |
| 40 | 5.00 | 4.69 | 6.36 | 6.87 | 8.86 | 15.01 | 19.73 | 12.36 | 1.43 |
| 45 | 7.50 | 9.42 | 11.01 | 12.62 | 11.87 | 15.23 | 18.78 | 12.57 | 1.35 |
| 50 | 5.30 | 9.58 | 13.67 | 16.46 | 14.95 | 13.95 | 15.60 | 10.88 | 1.29 |
| 55 | 0.91 | 3.22 | 11.30 | 17.35 | 15.39 | 13.04 | 12.91 | 9.30 | 1.31 |
| 60 | 6.40 | 5.66 | 12.03 | 16.19 | 17.70 | 14.92 | 13.01 | 8.96 | 1.80 |
| 65 | 10.37 | 12.89 | 17.42 | 16.62 | 18.22 | 12.51 | 10.97 | 5.29 | 1.23 |
| 70 | 14.14 | 13.02 | 18.05 | 20.18 | 12.62 | 7.01 | 0.85 | 2.28 | 0.48 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

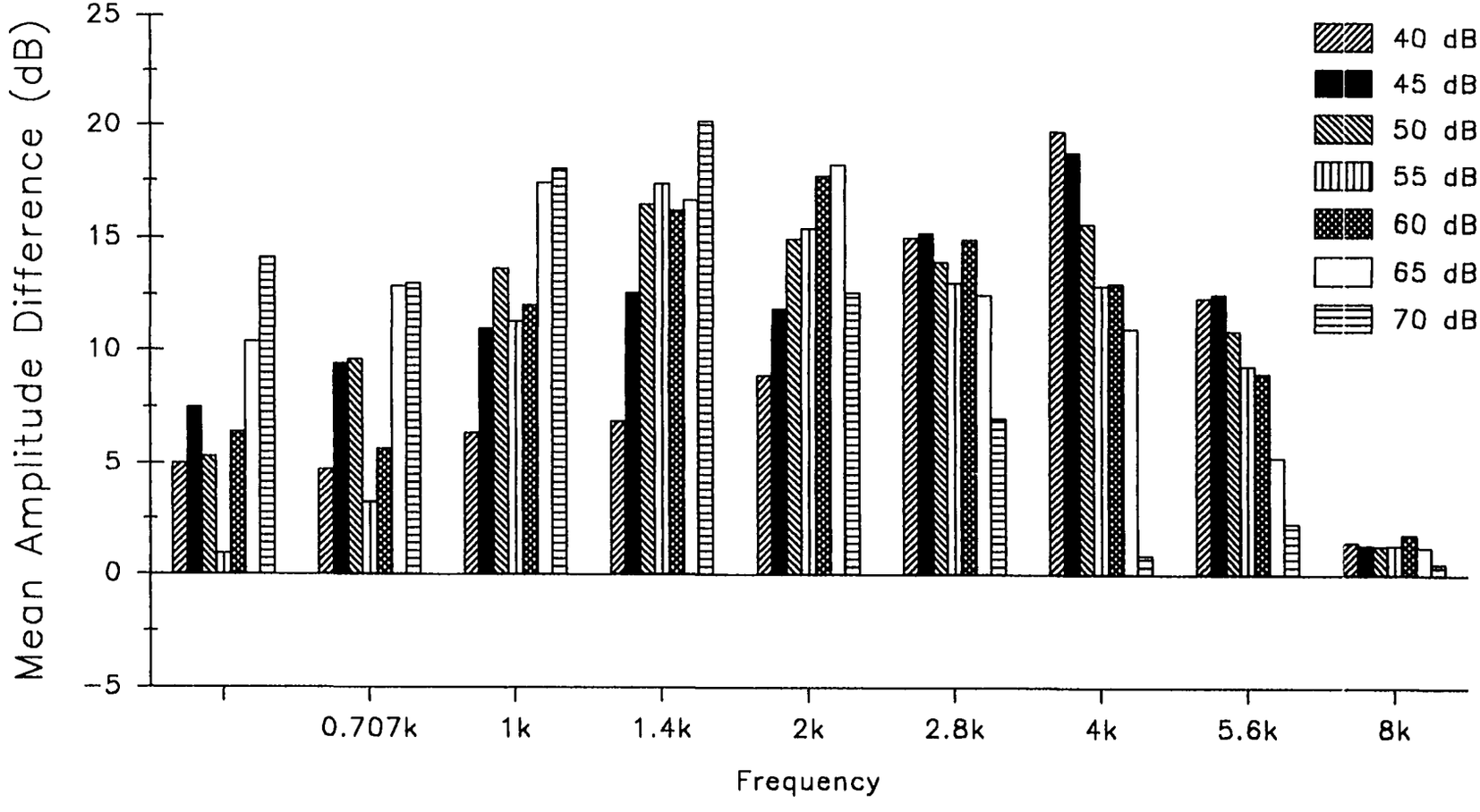


**Figure 8.** The effect of the interrupted conditioning/traumatizing noise exposure combination on normal DPOAE responses. Data are presented as the mean amplitude differences between the Aged Normal Group and the Interrupted Conditioning then Blast Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

representation of the mean amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero represent the magnitude of the amplitude reductions induced by the noise exposure, whereas the negative excursions from zero show where the magnitude of the DPOAE responses were actually larger in the exposed group than in the unexposed controls.

The overall shape of Figure 8 demonstrates the frequency-dependence of the noise-induced effects on the DPOAE responses. This pattern of change caused by the traumatizing noise exposure in animals previously sound conditioned on an interrupted schedule is similar to that obtained for the unconditioned animals (Figure 6). Although similar, there were differences in the DPOAE responses between the unconditioned (Blast Only) group and the sound conditioned (Interrupted Conditioning then Blast) group. These differences are discussed in detail in Section 5.3.3.2 as they relate to the possible protective role of the sound conditioning exposure.

### 5.3.3 Comparison of the effects of the traumatizing noise exposure on the DPOAE responses of unconditioned and sound conditioned animals -- Did sound conditioning provide protection?

When comparing the effects of the traumatizing noise exposure on the DPOAE amplitude growth function measured within the Blast Only Group, the Continuous Conditioning then Blast Group, and the Interrupted Conditioning then Blast Group, statistically significant differences were

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

found between the exposure groups (p=0.015). Results show that overall (data pooled over frequency and intensity), the Interrupted Conditioning then Blast was least affected by the traumatizing noise, followed closely by the Blast Only Group and then the Continuous Conditioning then Blast Group (see Table V, Results of the Tukey all pairwise multiple comparison test for the main effect of Group). This implies that there was some amount of protection afforded by prior sound conditioning with the interrupted moderate-level noise exposure used in this study. However, the overall effect of the continuous sound conditioning protocol seemed to render the auditory system more susceptible to the traumatizing noise exposure.

#### 5.3.3.1 Did continuous sound conditioning provide protection against the damaging effects of the traumatizing noise exposure?

In order to test the hypothesis that continuous sound conditioning provides protection against the damaging effects of the traumatizing noise exposure, the DPOAE responses of the Blast Only and the Continuous Conditioning then Blast Group were compared. The mean DPOAE amplitudes of the Continuous Conditioning then Blast Group were subtracted from the average DPOAE responses of Blast Only Group to quantify the differences between the groups. The mean DPOAE amplitude differences between the Continuous Conditioning then Blast Group and the Blast Only Group at each primary level and frequency are listed in Table 13. Figure 9 provides a graphical representation of the mean

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 13.** Mean amplitude difference data (in dB) between the Blast Only Group and the Continuous Conditioning then Blast Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | -0.10 | -0.55 | -0.32 | 0.03 | -0.05 | -0.23 | -0.25 | 0.09 | 0.47 |
| 25 | -0.09 | -0.46 | -0.26 | 0.09 | -0.35 | -0.15 | 0.57 | -0.48 | 1.00 |
| 30 | -0.69 | -0.28 | -0.22 | -0.81 | -0.10 | -0.56 | 0.16 | -0.94 | 2.12 |
| 35 | -0.50 | 0.00 | -0.51 | -0.08 | -0.07 | -0.16 | -0.15 | -1.60 | 1.70 |
| 40 | -0.15 | 0.09 | -0.82 | -0.02 | -0.57 | -0.07 | -0.70 | -1.50 | 1.64 |
| 45 | 0.23 | -0.07 | 0.42 | -0.26 | -0.09 | 0.54 | -0.75 | -0.88 | 1.53 |
| 50 | 0.15 | -0.38 | 0.11 | 0.25 | 0.23 | -0.05 | -0.60 | -3.29 | 2.39 |
| 55 | -0.06 | 0.01 | 2.06 | 2.27 | 1.59 | 0.55 | 0.19 | -2.16 | 0.19 |
| 60 | 1.36 | 0.01 | 3.15 | 3.18 | 1.88 | 0.24 | 0.05 | -0.12 | 0.70 |
| 65 | 4.27 | 0.20 | 2.54 | 3.82 | -1.27 | 1.15 | -0.26 | 0.35 | 0.69 |
| 70 | 5.19 | 1.44 | 3.11 | 3.45 | -5.25 | 1.72 | -0.71 | 0.59 | 0.74 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

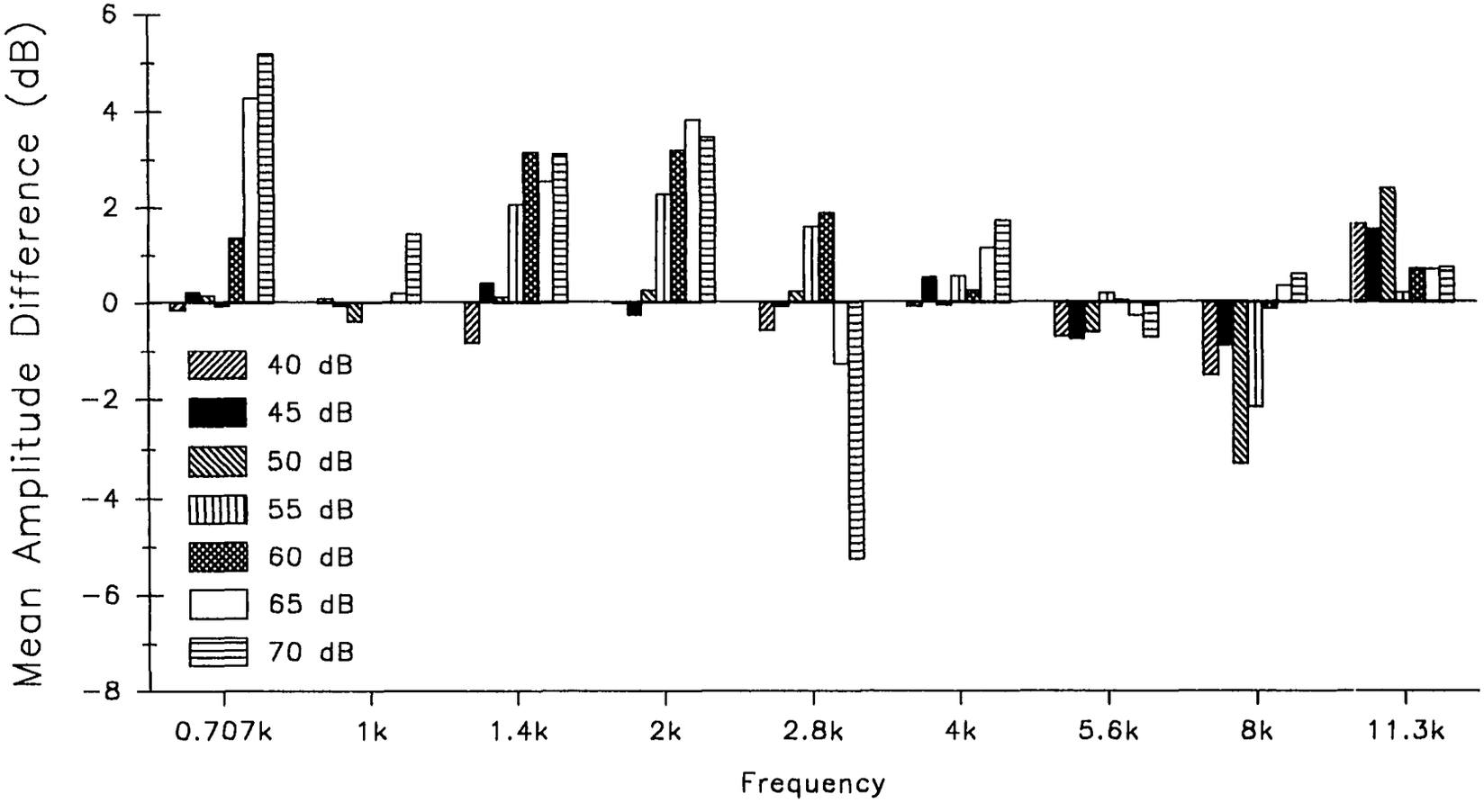


**Figure 9.** Comparison of the effect of the traumatizing noise on the DPOAE responses of the unconditioned vs. the continuous sound conditioned groups. Data are presented as the mean amplitude differences between the Blast Only Group and the Continuous Conditioning then Blast Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero represent an increased susceptibility to the traumatizing noise in the sound conditioned groups. This shows where (in terms of $f_2$ frequency and intensity) the sound conditioning acted to enhance the effects (DPOAE amplitude reductions) of the traumatic noise exposure rather than to protect against it. The negative excursions from zero show where the magnitudes of the DPOAE responses were actually larger in the sound conditioned groups than in the unconditioned control group. In other words, it is at these $f_2$ frequencies and corresponding primary tone levels that the sound conditioning appeared to provide protection against the subsequent traumatizing noise.

No exceptionally obvious pattern of protection was observed when comparing the DPOAE results of Blast Only Group and the Continuous Conditioning then Blast Group (Figure 9). This means that there were no real definite frequency regions that demonstrated that the conditioning noise was either helpful or harmful in protecting against the subsequent traumatic noise exposure. In addition, the amplitude differences between the two groups, for the most part, were fairly small, with maximum differences of 1-3 dB (on average). This finding is unusual given that the effects of continuous sound conditioning alone were more

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

damaging to the DPOAE responses than the interrupted protocol.

The lack of protection demonstrated here could possibly be related to the fact that the moderate-level continuous conditioning exposure chosen for study may have, by itself, been enough to cause irreversible damage to the outer hair cells, thus precluding the possibility of providing protection against the damaging effects of the subsequent traumatizing exposure. It was not determined whether or not this conditioning exposure had any residual effects on the DPOAE amplitude growth functions after the one week rest period that was given. However, it has been suggested that protection against subsequent noise trauma may be less likely to occur in the presence of a threshold shift induced by the sound conditioning exposure (Canlon et al, 1992; Ryan et al., 1994; Canlon and Fransson, 1995).

Canlon et al. (1992) demonstrated that protection against a subsequent traumatizing noise was not evident when the continuous sound conditioning paradigm used in their experiment caused a temporary threshold shift. When a group of rabbits was traumatized immediately following the conditioning exposure, the auditory brainstem response thresholds were better in the unconditioned control animals as compared with the sound conditioned animals (i.e., sound conditioning provided no protection). However, when another group of rabbits was given a two week rest period before being exposed to the traumatizing noise, the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

response measurements were better in the sound conditioned group of animals demonstrating the protective effect of the continuous conditioning exposure. Similar results were also reported by Ryan et al. (1994) who used gerbils as their experimental animals. These investigators found that a one week rest period was needed in between the continuous conditioning exposure and the traumatic noise exposure in order to eliminate the threshold shift caused by the conditioning and obtain protection against the subsequent noise trauma. The results of other continuous sound conditioning experiments showed that when the moderate-level conditioning noise did not cause any morphological or physiological alterations to the cochlea, no rest period was required before the subsequent traumatizing noise in order for a protective effect to exist (Canlon et al., 1988,1992; Canlon and Fransson, 1995).

Thus, it is possible that the continuous sound conditioning exposure used in this study (1-2 kHz; 89 dB SPL; presented continuously for 11 days) caused some degree of permanent damage to the region of the cochlea spanning the $f_2$ frequency range of interest. This may have resulted in the lack of any consistent and sizable protective effect due to prior sound conditioning with a continuous moderate-level noise.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

#### 5.3.3.2 Did interrupted sound conditioning provide protection against the damaging effects of the traumatizing noise exposure?

In order to test the hypothesis that interrupted sound conditioning provides protection against the damaging effects of the traumatizing noise exposure, the DPOAE responses of the Blast Only and the Continuous Conditioning then Blast Group were compared. The mean DPOAE amplitudes of the Interrupted Conditioning then Blast Group were subtracted from the average DPOAE responses of Blast Only Group to obtain the differences between the groups. The mean DPOAE amplitude differences between the Interrupted Conditioning then Blast Group and the Blast Only Group at each primary level and frequency are listed in Table 14. Figure 10 provides a graphical representation of the mean amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero represent an increased susceptibility to the traumatizing noise in the sound conditioned groups. This shows where (in terms of $f_2$ frequency and intensity) the sound conditioning acted to enhance the effects (DPOAE amplitude reductions) of the traumatic noise exposure rather than to protect against it. The negative excursions from zero show where the magnitudes of the DPOAE responses were actually larger in the sound conditioned groups than in the unconditioned control group. In other words, it is at these $f_2$ frequencies and corresponding primary tone

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 14.** Mean amplitude difference data (in dB) between the Blast Only Group and the Interrupted Conditioning then Blast Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | 0.27 | -0.33 | 0.32 | 0.47 | 0.20 | 0.61 | 0.22 | -0.10 | -0.02 |
| 25 | 0.24 | -0.13 | 0.30 | 0.80 | 0.12 | 0.68 | 0.80 | -0.67 | -0.37 |
| 30 | -0.11 | 0.01 | 0.15 | 0.12 | -0.22 | 0.31 | 0.72 | -1.76 | -1.03 |
| 35 | -0.03 | -0.06 | 0.23 | 0.54 | 0.10 | -0.06 | 0.64 | -2.80 | -1.86 |
| 40 | 0.61 | -0.03 | 0.37 | 0.93 | -0.22 | -0.17 | -0.75 | -4.07 | -2.62 |
| 45 | 1.11 | 0.45 | 0.89 | 0.55 | -0.13 | -2.03 | -1.01 | -4.13 | -3.14 |
| 50 | 2.23 | -0.01 | 2.45 | 1.86 | -0.33 | -4.12 | -1.28 | -6.32 | -3.19 |
| 55 | 2.73 | 1.14 | 4.45 | 3.93 | -0.73 | -5.09 | -1.10 | -4.16 | -1.37 |
| 60 | 3.75 | 1.38 | 5.20 | 4.90 | -0.08 | -4.89 | -0.94 | -2.17 | -0.01 |
| 65 | 4.15 | 1.41 | 4.79 | 4.48 | -2.42 | -3.57 | -1.39 | -3.52 | 0.00 |
| 70 | 1.92 | 2.12 | 5.35 | 4.75 | -4.88 | -0.22 | -1.95 | -2.37 | -1.02 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

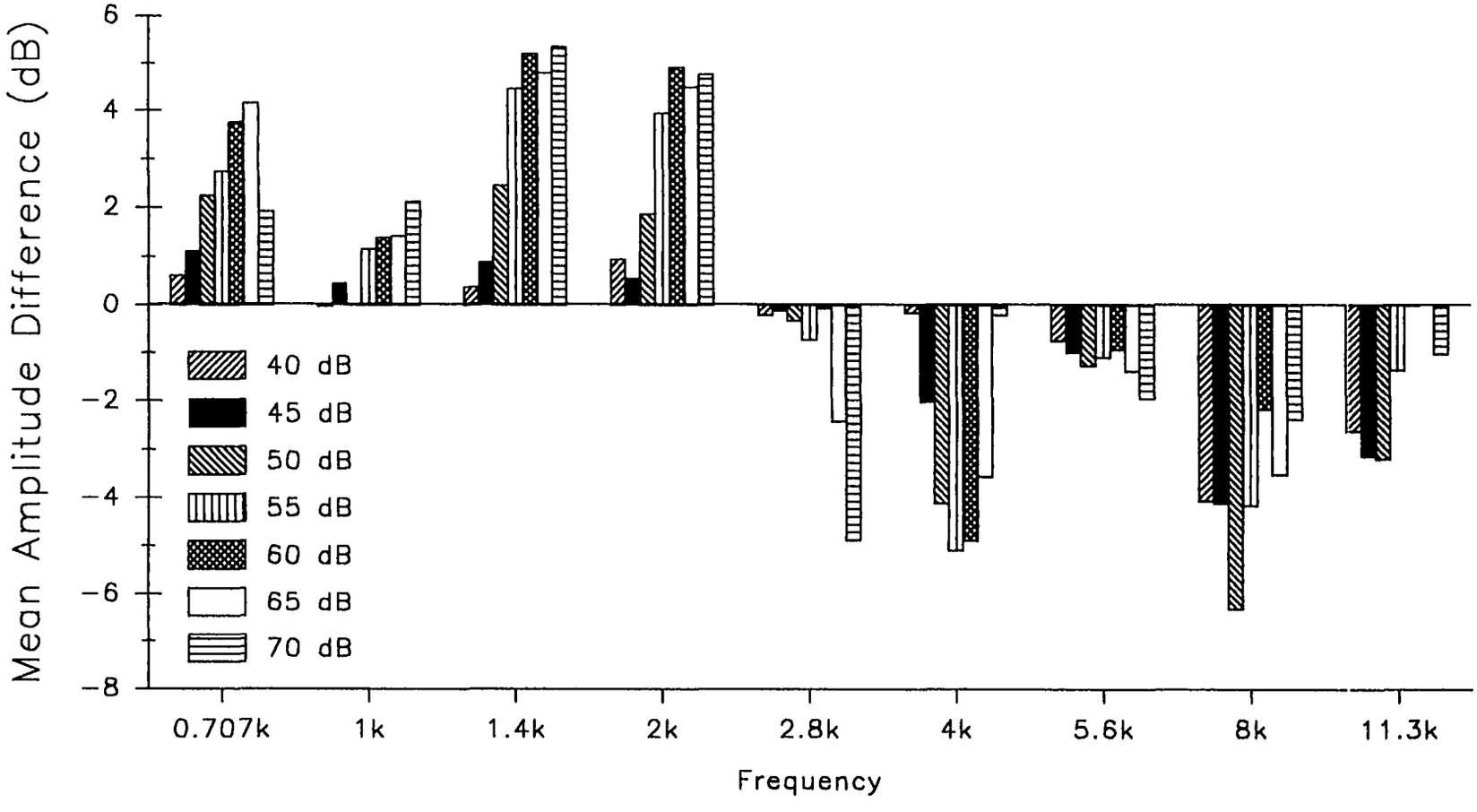


**Figure 10.** Comparison of the effect of the traumatizing noise on the DPOAE responses of the unconditioned vs. the interrupted sound conditioned groups. Data are presented as the mean amplitude differences between the Blast Only Group and the Interrupted Conditioning then Blast Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

levels that the sound conditioning appeared to provide protection against the subsequent traumatizing noise.

An interesting finding was observed when comparing the DPOAE results of the Blast Only Group and the Interrupted Conditioning then Blast Group. Figure 10 illustrates that interrupted sound conditioning produced a dual effect on the DPOAE responses depending upon the test frequency. The results revealed an apparent trend towards an increased susceptibility to the traumatizing noise exposure in the sound conditioned animals in the lower test frequency range ($f_2$ = 707-2000 Hz) and some degree of protection in the test frequency range spanning $f_2$ frequencies of 2828-11312 Hz. The differences between the groups were statistically significant at $f_2$ frequencies of 707-, 1000-, 8000-, and 11312 Hz ($P<0.05$). Still, although statistically significant differences were found in the two lowest and highest frequencies of $f_2$, it is the frequency-specific pattern showing where protection may or may not have occurred that is important and is worth further discussion.

The range of frequencies ($f_2$ = 707-2000 Hz) rendered more susceptible to the traumatizing noise exposure after prior sound conditioning with the interrupted moderate-level noise included within it the frequencies of the noise exposure band (1000-2000 Hz) and 707 Hz. In looking for an explanation for this finding, one might conclude that the increased susceptibility in the sound conditioned group may be the result of an additive effect between the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

noise-induced reductions in DPOAE amplitudes caused by the interrupted conditioning exposure alone and the reductions caused by exposure to the traumatizing noise. The interrupted sound conditioning exposure, when presented alone, had its maximum effect on the DPOAE amplitude growth functions measured when the frequency range of $f_2$ was 2000-4000 Hz (Figure 5). Smaller DPOAE amplitude reductions were found in at the $f_2$ frequencies 707-, 1000-, and 1414 Hz. Thus, this relatively simple explanation might hold true for the frequencies ranging from 707-2000 Hz.

However, also included in the frequency region of maximum DPOAE reductions caused by the interrupted conditioning noise are $f_2$ frequencies of 2828- and 4000 Hz. According to Figure 10, the DPOAEs generated by these $f_2$ frequencies were somewhat protected from the traumatizing noise exposure (more so at 4000- than at 2828 Hz). The amount of protection found was 5 dB or less. This tendency toward a protective effect as a result of prior sound conditioning was certainly unexpected given the magnitude of the DPOAE reductions (11-16 dB) at these frequencies after exposure to the sound conditioning exposure alone. One possible explanation for this result might be that at these particular frequencies, the noise-induced amplitude reductions caused by sound conditioning were only temporary, and full recovery of the amplitudes occurred within the 1 week rest period given prior to exposure to the traumatizing noise. Another explanation is that there

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

may be an overshoot in the recovery pattern of the DPOAE responses subsequent to the conditioning exposure such that there may be recovery to values better than baseline amplitudes. This overshoot phenomenon (or hyper-recovery) was reported by Kujawa and Liberman (1996) for frequencies within and slightly above the noise exposure band used to condition their guinea pigs (2-4 kHz). This overshoot in recovery after exposure to an interrupted moderate-level (conditioning) noise may be reflected as the protection that we see in the DPOAE amplitude growth functions at these frequencies.

The protective effects provided by the interrupted conditioning noise were also observed for DPOAEs generated by the highest frequencies of $f_2$ tested. Slight amplitude reductions occurred at $f_2$=5656 Hz in response to the conditioning noise, whereas there were virtually no noise-induced changes in the DPOAE amplitude growth functions at $f_2$ frequencies of 8000- and 11312 Hz caused by the interrupted conditioning noise.

The results of this study demonstrating the lack of protection in the frequency range encompassing the noise exposure band and the existence of protection in the frequency range above the noise exposure band in guinea pigs conditioned with an interrupted moderate-level noise have not been previously reported. The frequency-related pattern of protection which has been reported by other investigators usually shows that there <u>is</u> significant

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

protection from the subsequent traumatizing exposure afforded by prior sound conditioning with an interrupted protocol within the frequency region of the exposure band which further extends to higher frequencies (Campo et al., 1991; Henderson et al., 1992; Subramaniam et al., 1992, 1993). As mentioned earlier, the lack of protection demonstrated in this study for the lower frequency region (coinciding with the noise exposure band) could possibly be related to the fact that the moderate-level interrupted conditioning noise used may have, by itself, caused irreversible damage to the outer hair cells within this frequency region. Permanent damage to the cells within this region of the cochlea may have precluded the protective role of the sound conditioning exposure, and rendered the auditory system more susceptible to the deleterious effects of subsequent noise trauma. Again, as for the continuous conditioning protocol, it was not determined whether or not this interrupted conditioning exposure had any residual effects on the DPOAE amplitude growth functions after the one week rest period that was interposed between the conditioning and the traumatic exposures.

### 5.3.4 Comparison of the effects of the traumatizing noise exposure on the DPOAE responses of animals conditioned with continuous vs. interrupted moderate-level noise -- Is either sound conditioning protocol more protective?

The primary purpose of this study was to test the hypothesis that differences exist in the amount of protection provided by prior sound conditioning with

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

continuous versus interrupted moderate-level noise. In order to test this hypothesis, the average DPOAE responses of the Interrupted Conditioning then Blast Group and the Continuous Conditioning then Blast Group were compared. The mean DPOAE amplitudes of the Continuous Conditioning then Blast Group were subtracted from the average DPOAE responses of Interrupted Conditioning then Blast Group to quantify the differences between the groups. The mean DPOAE amplitude differences between the Continuous Conditioning then Blast Group and the Interrupted Conditioning then Blast Group at each primary level and frequency are listed in Table 15. Figure 11 provides a graphical representation of the mean amplitude differences between the two groups (in dB) plotted as a function of frequency for several different primary intensity levels (40-70 dB SPL). The positive excursions from zero show where (in terms of $f_2$ frequency and intensity) the magnitudes of the DPOAE responses of the Interrupted Conditioning then Blast Group were larger than the those measured in the Continuous Conditioning then Blast Group. The negative excursions from zero show where the magnitudes of the DPOAE responses were actually larger in the Continuous Conditioning then Blast Group than in the Interrupted Conditioning then Blast Group.

When comparing the effects of the traumatizing noise exposure on the DPOAE responses of the sound conditioned groups of animals, it was found that the group least

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 15.** Mean amplitude difference data (in dB) between the Interrupted Conditioning then Blast Group and the Continuous Conditioning then Blast Group

| Primary Level (dB) | Frequency (Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 707 | 1000 | 1414 | 2000 | 2828 | 4000 | 5656 | 8000 | 11312 |
| 20 | -0.37 | -0.22 | -0.64 | -0.44 | -0.25 | -0.84 | -0.47 | 0.19 | 0.49 |
| 25 | -0.33 | -0.33 | -0.56 | -0.71 | -0.47 | -0.83 | -0.23 | 0.19 | 1.37 |
| 30 | -0.58 | -0.29 | -0.37 | -0.93 | 0.12 | -0.87 | -0.56 | 0.82 | 3.15 |
| 35 | -0.47 | 0.06 | -0.74 | -0.62 | -0.17 | -0.10 | -0.79 | 1.20 | 3.56 |
| 40 | -0.76 | 0.12 | -1.19 | -0.95 | -0.35 | 0.10 | 0.05 | 2.57 | 4.26 |
| 45 | -0.88 | -0.52 | -0.47 | -0.81 | 0.04 | 2.57 | 0.26 | 3.25 | 4.67 |
| 50 | -2.08 | -0.37 | -2.34 | -1.61 | 0.56 | 4.07 | 0.68 | 3.03 | 5.58 |
| 55 | -2.79 | -1.13 | -2.39 | -1.66 | 2.32 | 5.64 | 1.29 | 2.00 | 1.56 |
| 60 | -2.39 | -1.37 | -2.05 | -1.72 | 1.96 | 5.13 | 0.99 | 2.05 | 0.71 |
| 65 | 0.12 | -1.21 | -2.25 | -0.66 | 1.15 | 4.72 | 1.13 | 3.87 | 0.69 |
| 70 | 3.27 | -0.68 | -2.24 | -1.30 | -0.37 | 1.94 | 1.24 | 2.96 | 1.76 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

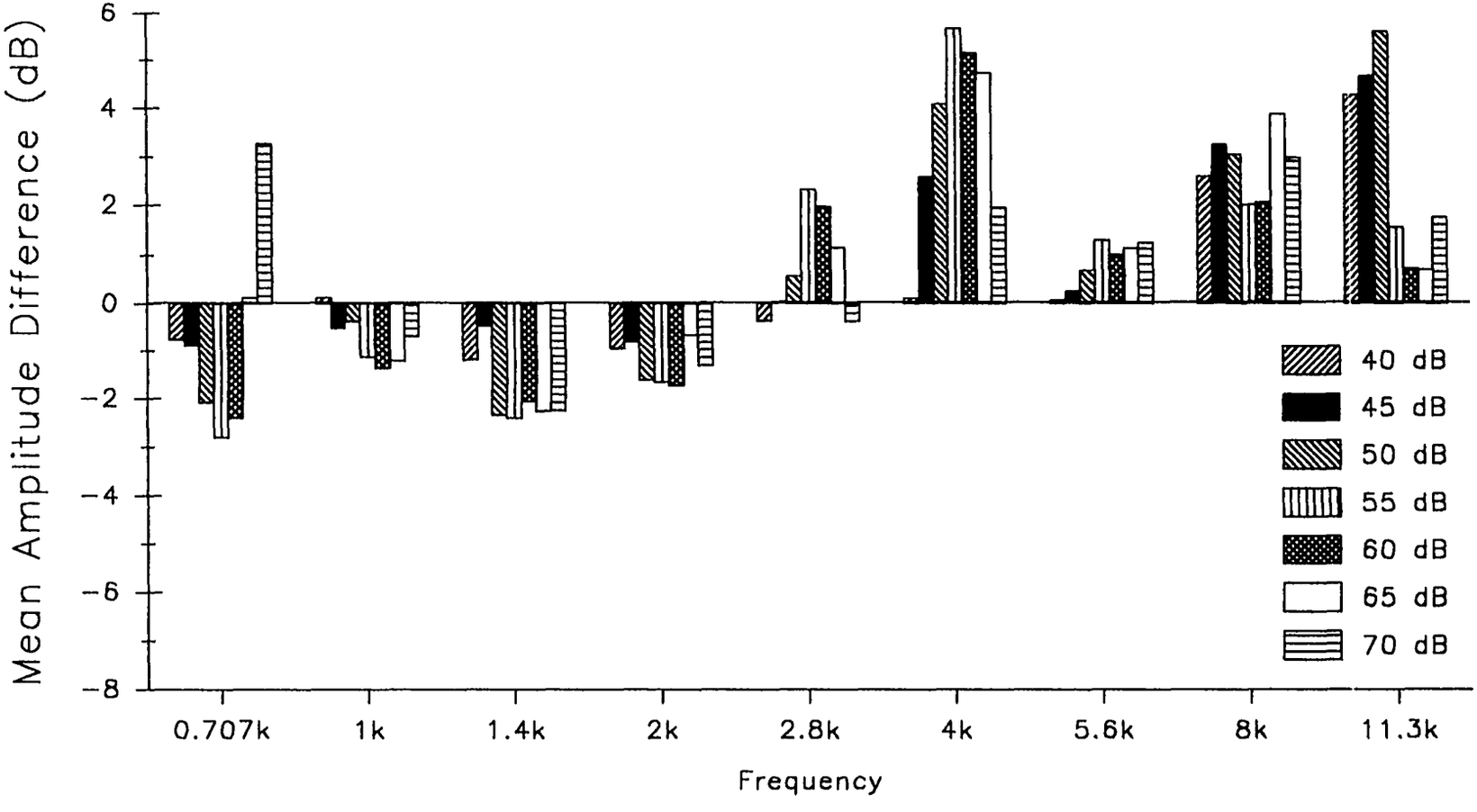


**Figure 11.** Comparison of the effects of the traumatizing noise exposure on the DPOAE responses of animals conditioned with continuous vs. interrupted moderate-level noise. Data are presented as the mean amplitude differences between the Interrupted Conditioning then Blast Group and the Continuous Conditioning then Blast Group (in dB) plotted as a function of frequency (0.707-11.312 kHz) for several different primary intensity levels (40-70 dB SPL; inset).

affected by the high-level noise depended upon the frequency of $f_2$ being tested (see Figure 11). Specifically, for low frequencies ($f_2$=707-, 1000-, 1414-, and 2000 Hz), the DPOAE amplitudes of the Continuous Conditioning then Blast Group were greater than those measured in the Interrupted Conditioning then Blast Group. The amplitude differences ranged from approximately 2-3 dB at 707- and 1414 Hz and 1-2 dB at 1000- and 2000 Hz. These differences were statistically significant at 707- and 1000 Hz ($P<0.05$). Thus, within this low frequency region, the results suggest that traumatizing noise produced slightly more damage in the animals previously conditioned with the interrupted schedule of moderate-level noise. At higher frequencies of $f_2$ (2828-11,312 Hz), however, smaller amplitude reductions were found in the DPOAE responses of the Interrupted Conditioning then Blast Group as compared with the reductions measured in the Continuous Conditioning then Blast Group. The amplitude differences between the two sound conditioned groups ranged from approximately 1-2 dB at 2828- and 5656 Hz and 2-6 dB at 4000-, 8000-, and 11312 Hz. These differences were statistically significant at 8000- and 11312 Hz ($P<0.05$). Thus, the results suggest that the damaging effects of the traumatizing noise were smaller in the animals previously conditioned with the interrupted schedule of moderate-level noise within this higher frequency range.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

As discussed earlier, it was within the high frequency range that a protective effect was found for animals exposed to the interrupted sound conditioning protocol used in this study (see Figure 10). However, no real definite frequency regions were identified that demonstrated that the continuous sound conditioning protocol was either helpful or harmful in protecting against the subsequent traumatic noise exposure (see Figure 9). Therefore, the results of this study suggest that the interrupted sound conditioning protocol was more effective than the continuous conditioning protocol in providing protection against the damaging effects of a subsequent traumatic noise exposure for certain frequencies of $f_2$.

There have been other attempts to compare the effectiveness of the two different schedules of moderate-level conditioning noise (Fowler et al., 1995; White et al., 1996). However, neither of these investigations produced results which demonstrated that the conditioning protocols used provided any degree of protection against the permanent damage caused by the subsequent traumatizing noise. Fowler et al. (1995) used various continuous and interrupted sound conditioning protocols within their study examining the effects of noise trauma in unconditioned and sound conditioned mice. However, there did not appear to be any real systematic attempt made to match the exposures for their energy content. In looking closer at their conditioning protocols, there was one continuous exposure

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

protocol (86 dB SPL narrowband noise centered at 4.5 kHz presented continuously for 10 days) and one interrupted exposure protocol (96 dB SPL noise with the same spectral characteristics presented 6 hours per day for 10 days) used in which a 5-dB trading rule might have been implemented to match the energies of the exposures. However, this was not stated explicitly. Further, neither conditioning protocol was effective in providing protection against the subsequent traumatic exposure. For the most part, the conditioned animals demonstrated slightly higher permanent threshold shifts that the unconditioned animals exposed to the same traumatic stimulus.

White et al. (1996) did appear to make a conscious effort in selecting their continuous and interrupted sound conditioning protocols in order to equate the energy content of the two exposure schedules. These investigators followed a 3 dB time-intensity trading rule similar to that used in the present study. However, when auditory brainstem response thresholds and DPOAE amplitudes were recorded 30 days following the traumatic exposure, both of the sound conditioned groups, as well as the unconditioned control group, demonstrated similar amounts of permanent threshold shift and equal reductions in DPOAE amplitudes.

Thus, the results of the present study suggest that overall, there were significant differences in the degree of protection provided by prior sound conditioning with continuous vs. interrupted schedules of moderate-level

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

noise of equal acoustic energy. Given the noise exposure protocols chosen for study, it appears that the interrupted sound conditioning protocol provided more protection against the damaging effects of the subsequent traumatic exposure than the continuous conditioning protocol. While no real definite frequency regions were identified demonstrating that continuous sound conditioning was either helpful or harmful in protecting against the subsequent traumatic noise exposure (see Figure 9), the effectiveness of the interrupted sound conditioning protocol in providing protection was highly frequency-dependent. In the frequency range encompassing the noise exposure band and extending down to ½ octave below the lower cutoff frequency ($f_2$ = 707-2000 Hz), neither sound conditioning exposure was effective in providing protection against the subsequent traumatizing exposure when the DPOAE responses were compared with those obtained in the unconditioned group. However, when the frequencies of $f_2$ generating the DPOAEs were limited to the frequency region above that of the noise exposure band, the results indicate that some degree of protection was afforded by the interrupted sound conditioning protocol.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

# CHAPTER 6

## SUMMARY AND CONCLUSIONS

The primary purpose of this study was to test the hypothesis that differences exist in the amount of protection provided by prior sound conditioning with continuous versus interrupted schedules of moderate-level noise of equal acoustic energy. Differences were determined by monitoring the changes that occurred in distortion product otoacoustic emission (DPOAE) amplitude growth functions after a subsequent higher level traumatizing exposure in guinea pigs (*Cavia cobaya*) conditioned with either continuous or interrupted noise. The results suggest that overall, there were significant differences in the degree of protection provided by prior sound conditioning with the continuous and interrupted schedules of moderate-level noise used in this study. Specifically, there was some degree of protection afforded by prior sound conditioning with the interrupted noise protocol. The frequency region where protection was found, however, was limited to the region above that of the noise exposure band. Conversely, there was a lack of any consistent and sizable protective effect found across the entire test frequency range when the continuous conditioning protocol was used as the moderate-level exposure. Therefore, while neither conditioning protocol was effective in providing protection against damaging effects of the subsequent traumatizing exposure in the low



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

frequency range (frequencies encompassing the noise exposure band and extending down to ½ octave below the lower cutoff frequency), the interrupted sound conditioning protocol was more effective than the continuous conditioning protocol in the frequency region above that of the noise exposure band.

One possible reason for the lack of protection found in this study in response to prior sound conditioning (across most test frequencies for the continuous conditioning protocol and in the frequency region encompassing the noise exposure band for the interrupted conditioning protocol) is that the moderate-level conditioning exposures may have, by themselves, caused irreversible damage to the outer hair cells within the test frequency region. Permanent damage to the outer hair cells within this region of the cochlea may have precluded the protective role of the sound conditioning exposures, and rendered the auditory system more susceptible to the deleterious effects of the subsequent noise trauma. This explanation is supported by the findings of Canlon et al. (1992) which suggested that protection against subsequent noise trauma was less likely to occur in the presence of a threshold shift induced by the sound conditioning exposure. It was not determined whether or not the sound conditioning protocols used in the present study had any residual effects on the DPOAE responses after the one week rest period that was given in between the conditioning and the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

traumatic exposures. Future experiments will include the addition of exposure groups whose DPOAE responses will be measured after the one week rest period so that information can be obtained about the condition of the outer hair cells just prior to the traumatic noise exposure.

Many investigators have studied the protective effect of different schedules of moderate-level noise on the auditory system in a variety of animal species (guinea pigs, Canlon et al., 1988, 1992; Canlon and Fransson, 1995; rabbits, Canlon et al., 1992; chinchillas, Campo et al., 1991; Henderson et al., 1992 Subramaniam et al., 1992, 1993a,b; gerbils, Ryan et al., 1994; mice, Fowler et al., 1995). Both continuous and interrupted schedules of moderate-level noise have been shown to be effective in providing protection against the damaging effects of subsequent noise trauma. However, there have also been reports suggesting that similar schedules (continuous and interrupted) of moderate-level noise exposure, in some cases, render the auditory system more susceptible to the ototoxic effects of the higher-level subsequent exposure. The results of the present study <u>again</u> support the protective role of an interrupted sound conditioning exposure protocol. However, unlike the findings of other studies using similar conditioning protocols (Campo et al., 1991; Henderson et al., 1992; Subramaniam et al., 1993a), the effectiveness of the interrupted moderate-level noise exposure in providing protection was highly

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

frequency-dependent, limited only to the frequency region above that of the noise exposure band. In addition, while other investigators have demonstrated the protective role of continuous sound conditioning (Canlon et al., 1988, 1992; Ryan et al., 1994; Canlon and Fransson, 1995), the results of this study do not support their findings.

Given the disparate findings of this and other studies, it appears that the protective effect of prior sound conditioning with moderate-level noise is not a very straightforward phenomenon and is highly dependent on the noise exposure conditions (e.g. frequency, duration, intensity), animal species, and response measurements (e.g. behavioral thresholds, auditory brainstem response thresholds, DPOAE amplitudes) studied. Additional studies are needed so that a better understanding of the ideal exposure conditions for achieving noise-induced resistance to hearing loss can be obtained. Before such details are worked out, the use of a protocol which incorporates the prophylactic use of low-to-moderate level noise for the prevention of noise-induced hearing loss would be impractical.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

## REFERENCES


Ahroon, W. A., Hamernik, R. P., and Davis, R. I. (1993). Complex noise exposures: An energy analysis. J. Acoust. Soc. Am. 93, 997-1006.

Allen, J. B., and Fahey, P. F. (1993). A second cochlear-frequency map that correlates distortion product and neural tuning measurements. J. Acoust. Soc. Am. 94, 809-816.

Altschuler, R. A., Lim, H. H., Ditto, J., Dolan, D., and Raphael, Y. (1996). Protective mechanisms in the cochlea: Heat shock proteins. In: R. J. Salvi, D. Henderson, F. Fiorino, and V. Colletti (Eds.), Auditory System Plasticity and Regeneration, Thieme Medical Publishers, Inc., New York, pp. 202-212.

American Veterinary Medical Association (1993). Report of the AVMA Panel on Euthanasia. J. Am. Vet. Med. Assoc. 202, 230-249.

Atherley, G. R. C. (1973). Noise-induced hearing loss: The energy principle for recurrent impact noise and noise exposure close to the recommended limits. Ann. Occup. Hyg. 16, 183-192.

Atherley, G. R. C., and Martin, A. M. (1971). Equivalent continuous noise level as a measure of injury from impact and impulse noise. Ann. Occup. Hyg. 14, 11-19.

Barbe, M. F., Tytell, M., Gower, D. J., and Welsh, W. J. (1988). Hyperthermia protects against light damage in the rat retina. Science 241, 1817-1820.

Barone, J. A., Peters, J. M., Garabrant, D. H., Bernstein, L., and Krebsbach, R. (1987). Smoking as a risk factor in noise-induced hearing loss. J. Occup. Med. 29, 741-745.

Barrenäs, M. -L., and Hellström, P. -A. (1996). The effect of low level acoustic stimulation on susceptibility to noise in blue- and brown-eyed young human subjects. Ear and Hear. 17, 63-68.

Barrenäs, M. -L., and Lindgren, F. (1990). The influence of inner ear melanin on susceptibility to TTS in humans. Scand. Audiol. 19, 97-102.

Boettcher, F. A., and Schmiedt, R. A. (1995). Distortion-product otoacoustic emissions in Mongolian gerbils with resistance to noise-induced hearing loss. J. Acoust. Soc. Am. 98, 3215-3222.




Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Boettcher, F. A., Spongr, V. P., and Salvi, R. J. (1992). Physiological and histological changes associated with the reduction in threshold shift during interrupted noise exposure. Hear. Res. 62, 217-236.

Bohne, B. A., and Clark, W. W. (1982). Growth of hearing loss and cochlear lesion with increasing duration of noise exposure. In: R. P. Hamernik, D. Henderson, and R. Salvi (Eds.), New Perspectives on Noise-induced Hearing Loss, Raven Press, New York, pp. 283-302.

Bohne, B. A., Yohman, L., and Gruner, M. M. (1987). Cochlear damage following interrupted exposures on hearing loss from traumatic exposure. Hear. Res. 55, 195-200.

Bohne, B. A., Zahn, S. J., and Bozzay, D. (1985). Damage to the cochlea following interrupted exposure to low frequency noise. Ann. Otol. Rhinol. and Laryngol. 94, 122-128.

Borg, E., and Nilsson, R. (1984). Acoustic reflex in industrial noise. In: S. Silman (Ed.), The Acoustic Reflex. Basic principles and clinical applications. Academic Press, New York, pp. 413-440.

Brown, A. M. (1987). Acoustic distortion from rodent ears: A comparison of responses from rats, guinea pigs and gerbils. Hear. Res. 31, 25-38.

Brown, A. M., and Gaskill, S. A. (1990). Measurement of acoustic distortion reveals underlying similarities between human and rodent mechanical responses. J. Acoust. Soc. Am. 88, 840-849.

Brown, A. M., Gaskill, S. A., and Williams, D. M. (1992). Mechanical filtering of sound in the inner ear. Proc. R. Soc. Lond. B 250, 29-34.

Brown, A. M., McDowell, B., and Forge, A. (1989). Effects of chronic gentamicin treatment on hair cells can be monitored using acoustic distortion products. Hear. Res. 42, 143-156.

Burns, W., and Robinson, D. W. (1970). Hearing and Noise in Industry. Her Majesty's Stationery Office, London, England.

Byrne, C., Henderson, D., Saunders, S., Powers, N., and Farzi, F. (1988). Interaction of noise and whole body vibration. In: O. Manninen (Ed.), Recent Advances in Research on the Combined Effects of Environmental Factors, ISCES, Finland, pp. 239-254.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Campo, P., Subramaniam, M., and Henderson, D. (1991). The effect of "conditioning" exposures on hearing loss from traumatic exposure. Hear. Res. 55, 195-200.

Canlon, B., Borg, E., and Flock, Å. (1988). Protection against noise trauma by pre-exposure to a low level acoustic stimulus. Hear. Res. 34, 197-200.

Canlon, B., Borg, E., and Löfstrand, P. (1992). Physiologic and morphologic aspects of low-level acoustic stimulation. In: A. Dancer, D. Henderson, R. J. Salvi, R. P. Hamernik (Eds.), Noise-Induced Hearing Loss, Mosby Year Book, St. Louis, MO, pp. 489-499.

Canlon, B., and Fransson, A. (1994). Sound conditioning modulates calbindin D-28 kDa immunoreactivity in the cochlea. Abstracts of the 17th Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg Beach, Florida, p. 66.

Canlon, B., and Fransson, A. (1995). Morphological and functional preservation of the outer hair cells from noise trauma by sound conditioning. Hear. Res. 84, 112-124.

Canlon, B., Löfstrand, P., and Borg, E. (1993). Ultrastructural changes in the presynaptic region of outer hair cells after acoustic stimulation. Neurosci. Lett. 150, 103-106.

Carder, H. M., and Miller, J. D. (1972). Temporary threshold shifts from prolonged exposure to noise. J. Speech Hear. Res. 15, 603-623.

Carlin, M. F., and McCrosky, R. L. (1980). Is the eye color a predictor of noise induced hearing loss? Ear and Hear. 1, 191-196.

Carter, N. L. (1980). Eye color and susceptibility to noise induced permanent threshold shift. Audiol. 19, 86-93.

Center for Disease Control (1983). Leading work-related diseases and injuries - United States. In: Morbidity and Mortality Weekly Report, 32, 24-26.

Christakos, S., Gabrielides, C., and Rhoten, W. B. (1989). Vitamin D-dependent calcium binding proteins: chemistry, distribution, functional considerations, and molecular biology. Endocr. Rev. 10, 3-26.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Clark, W. W., and Bohne, B. A. (1978). Animal model for the 4 kHz tonal dip. Ann. Otol. Rhinol. and Laryngol. (Suppl. 51) 87, 1-16.

Clark, W. W., and Bohne, B. A. (1987). Hearing loss and damage to the cochlea following continuous and interrupted exposure to low-frequency noise. In: Abstr. 10th Midwinter Res. Meeting of the Assoc. Res. Otolaryngol., pp. 9-10.

Clark, W. W., Bohne, B. A., and Boettcher, F. A. (1987). Effect of periodic rest on hearing loss and cochlear damage following exposure to noise. J. Acoust. Soc. Am. 82(4), 1253-1264.

Cody, A. R., and Johnstone, B. M. (1982). Temporary threshold shift modified by binaural acoustic stimulation. Hear. Res. 6, 199-205.

Dagli, S., and Canlon, B. (1995). Protection against noise trauma by sound conditioning in the guinea pig appears not to be mediated by the middle ear muscles. Neurosci. Lett. 194, 57-60.

Davis, H., Morgan, C. T., Hawkins, J. E., Jr. (1943). Temporary deafness following exposure to loud tones and noise. Acta Otolaryngol. Suppl. 88.

Dechesne, C. J., Kim, H. N., Nowak, T. S., Jr., and Wenthold, R. J. (1992). Expression of heat shock protein, HSP 72, in guinea pig and rat cochlea after hyperthermia: immunochemical and in situ hybridization analysis. Hear. Res. 59, 195-204.

Ditto, J. L., Raphael, Y., Lim, H. H., Wang, Y., and Altschuler, R. A. (1994). Stress shock response in the rat cochlea: Noise induced expression of HSP 27. Abstracts of the 17th Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg Beach, Florida, p. 121.

Eldred, K. M., Gannon, W., and von Gierke, H. E. (1955). Criteria for short time exposure of personnel to high intensity jet aircraft noise. W.A.D.C. TN 55-355, Aero Space Medical Lab Wright Patterson A.F.B.

Engström, H., Ades, H. W., and Bredberg, G. (1970). Normal structure of the organ of Corti and the effect of noise-induced cochlear damage. In: G. E. W. Walstenholm, and J. Knight (Eds.), Senscrineural Hearing Loss, Churchill, London, pp. 127-152.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Engström, H., and Engström, B. (1979). Structural changes in the cochlea following overstimulation by noise. Acta Otolaryngol. Suppl. 360, 75-79.

Environmental Protection Agency, Office of Noise Abatement and Control (1981). Noise in America: The extent of the noise Problem (EPA Report No. 550/9-81-191). Washington, D.C.

Erostegui, C., Norris, C. H., and Bobbin, R. P. (1994). In vitro pharmacologic characterization of a cholinergic receptor on guinea pig outer hair cells. Hear. Res. 74, 135-147.

Fowler, T., Canlon, B., Dolan, D., and Miller, J. M. (1995). The effect of noise trauma following training exposures in the mouse. Hear. Res. 88, 1-13.

Franklin, D. J., Lonsbury-Martin, B. L., Stagner, B. B., and Martin, G. K. (1991). Altered susceptibility of $2f_1$-$f_2$ acoustic-distortion products to the effects of repeated noise exposure in rabbits. Hear. Res. 53, 185-208.

Fredelius, L., and Wersäll, J. (1992). Hair cell damage after continuous and interrupted pure tone overstimulation: A scanning electron microscopic study in the guinea pig. Hear. Res. 62, 194-198.

Gratton, M. A., Salvi, R. J., Kamen, B. A., and Saunders, S. S. (1990). Interaction of cisplatin and noise on the peripheral auditory system. Hear. Res. 50, 211-224.

Guberan, E., Fernandez, J., Gardiner, J., and Terrier, G. (1971). Hazardous exposure to industrial impact noise: Persistent effect on hearing. Ann. Occup. Hyg. 14, 345-350.

Hamernik, R. P., Henderson, D., Crossley, J. J., and Salvi, R. J. (1974). Interaction of continuous and impulse noise: Audiometric and histological effects. J. Acoust. Soc. Am. 55, 117-121.

Hamernik, R. P., Turrentine, G., Roberto, M., Salvi, R. J., and Henderson, D. (1984). Anatomical correlates of impulse noise-induced mechanical damage in the cochlea. Hear. Res. 13, 229-247.

Henderson, D., Campo, P., Subramaniam, M., and Fiorino, F. (1992). Development of resistance to noise. In: A. Dancer, D. Henderson, R. J. Salvi, R. P. Hamernik (Eds.), Noise-Induced Hearing Loss, Mosby Year Book, St. Louis, MO, pp. 476-488.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Henderson, D., Subramaniam, M., Gratton, M. A., and Saunders, S. S. (1991). Impact noise: The importance of level, duration, and repetition rate. J. Acoust. Soc. Am. 89, 1350-1357.

Henderson, D., Subramaniam, M., Papazian, M., and Spongr, V. P. (1994). The role of middle ear muscles in the development of resistance to noise induced hearing loss. Hear. Res. 74, 22-28.

Henry, K. R. (1983). Lifelong susceptibility to acoustic trauma: changing patterns of cochlear damage over the life span of the mouse. Audiology 22, 372-383.

Henselman, L. W., Henderson, D., Subramaniam, M., and Sallustio, V. (1994). The effect of "conditioning" exposures on hearing loss from impulse noise. Hear. Res. 78, 1-10.

Hunt, W. J., Hamernik, R. P., and Henderson, D. (1976). The effects of impulse level on the interaction between impulse and continuous noise. Trans. Am. Acad. Opthalmol. Otolaryngol. 82, 305-308.

Hutter, M. M., Sievers, R. E., Barbosa, V., and Wolfe, C. L. (1994). Heat-shock protein induction in rat hearts. A direct correlation between the amount of heat shock protein induced and the degree of myocardial protection. Circulation 89, 355-360.

International Standards Organization (1981). Acoustic-determination of occupational noise exposure and estimation of noise-induced hearing impairment. ISO 1999, Geneva, Switzerland.

Kemp, D. T. (1979). Evidence of mechanical nonlinearity and frequency selective wave amplification in the cochlea. Arch. Otol. Rhinol. Laryngol. 224, 37-45.

Kim, D. O. (1980). Cochlear mechanics: Implications of electrophysiological and acoustical observations. Hear. Res. 2, 297-317.

Kim, D. O., Leonard, G., Smurzynski, J., and Jung, M. D. (1992). Otoacoustic emissions and noise-induced hearing loss: Human studies. In: A. Dancer, D. Henderson, R. J. Salvi, R. P. Hamernik (Eds.), Noise-Induced Hearing Loss, Mosby Year Book, St. Louis, MO, pp. 98-105.

Kleinstein, R. N., Seitz, M. R., Barton, T. E., and Smith, C. R. (1984). Iris color and hearing loss. Am. J. Optom Physiol. Opt. 61, 145-149.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Kujawa, S. G., Glattke, T. J., Fallon, M., and Bobbin, R. P. (1992). Intracochlear application of acetylcholine alters sound-induced mechanical events within the cochlear partition. Hear. Res. 61, 106-116.

Kujawa, S. G., Glattke, T. J., Fallon, M., and Bobbin, R. P. (1993). Contralateral sound suppresses distortion product otoacoustic emissions through cholinergic mechanisms. Hear. Res. 68, 97-106.

Kujawa, S. G., Glattke, T. J., Fallon, M., and Bobbin, R. P. (1994). A nicotinic-like receptor mediates suppression of distortion product otoacoustic emissions by contralateral sound. Hear. Res. 74, 122-134.

Kujawa, S. G., and Liberman, M. C. (1996). Sound conditioning enhances cochlear responses in guinea pig. In: G. R. Popelka, Ph.D. (Ed.), Abstracts of the Nineteenth Midwinter Research Meeting, Association for Research in Otolaryngology, St. Petersburg Beach, Florida, p. 34.

Kuzniarz, J. J., Swierczynski, Z., and Lipowczan, A. (1976). Impulse noise induced hearing loss in industry and the energy concept: A field study. In: Proceedings of B. S. A. Second Conference, Southampton, England (Academic Press, London).

Li, H. -S., and Borg, E. (1991). Age-related loss of auditory sensitivity in two mouse genotypes. Acta Otolaryngol. (Stockh) 111, 827-834.

Liberman, M. C. (1992). Does olivocochlear feedback protect the cats's inner ear from acoustic injury? In: A. Dancer, D. Henderson, R. J. Salvi, R. P. Hamernik (Eds.), Noise-Induced Hearing Loss, Mosby Year Book, St. Louis, MO, pp. 423-428.

Liberman, M. C., and Kiang, N. Y.-S. (1978). Acoustic trauma in cats: Cochlear pathology and auditory-nerve activity. Acta Otolaryngol. Suppl. 358, 1-63.

Lim, D. J., and Dunn, D. E. (1979). Anatomic correlates of noise induced hearing loss. Otolaryng. Clin. North Am. 12, 493-513.

Lim, H. H., Jenkins, O. H., Myers, M. W., Miller, J. M., and Altschuler, R. A. (1993). Detection of HSP 72 synthesis after acoustic overstimulation in the rat cochlea. Hear. Res. 69, 146-150.

Lim, H. H., Miller, J. M., Dolan, D., Raphael, Y., and Altschuler, R. A. (1996). Noise-induced expression of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

heat shock proteins in the cochlea. In: A. Axelsson, H. M. Borchgrevink, R. P. Hamernik, P. -A. Hellström, D. Henderson, and R. J. Salvi (Eds.), Scientific Basis of Noise-Induced Hearing Loss, Thieme Medical Publishers, Inc., New York, pp. 43-49.

Lim, H. H., Moon, A., Wang, Y., Moran, A., and Altschuler, R. A. (1994). Stress shock response in the rat cochlea: Noise induced increased expression of HSP 90. Abstracts of the 17th Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg Beach, Florida, p. 67.

Lindquist, S., and Craig, E. A. (1988). The heat shock protein. Annu. Rev. Genet. 22, 631-677.

Martin, A. (1976). The equal energy concept applied to impulse noise. In: D. Henderson, R. P. Hamernik, D. S. Dosanjh, and J. H. Mills (Eds.), Effects of Noise on Hearing, Raven Press, New York, pp. 421-453.

Matthews, J. W., and Molnar, C. E. (1986). Modeling of intracochlear and ear canal distortion product $2f_1$-$f_2$. In: J. B. Allen, J. L. Hall, A. Hubbard, S. T. Neely, and A. Tubis (Eds.), Peripheral Auditory Mechanisms, Springer-Verlag, New York, pp. 258-265.

McFadden, D. (1986). Some issues associated with interactions between ototoxic drugs and exposure to intense sounds. In: R. J. Salvi, D. Henderson, R. P. Hamernik, and V. Colletti (Eds.), Basic and applied aspects of noise-induced hearing loss. Nato Sci Series A: Vol. III Life Sciences, London: Plenum Press, New York, pp. 541-550.

McFadden, D., and Plattsmier, H. S. (1983). Aspirin can potentiate the temporary hearing loss induced by intense sounds. Hear. Res. 9, 295-316.

Melnick, W. (1976). Human asymptotic threshold shift. In: D. Henderson, R. P. Hamernik, D. S. Dosanjh, and J. H. Mills (Eds.), Effects of Noise on Hearing, Raven Press, New York, pp. 277-289.

Miller, J. D., Watson, C. S., and Covell, W. P. (1963). Deafening effects of noise on the cat. Acta Otolaryngol. (Suppl.) 176, 1-91.

Mills, D, M., Norton, S. J., and Rubel, E. W. (1993). Vulnerability and adaptation of distortion-product otoacoustic emissions to endocochlear potential variation. J. Acoust. Soc. Am. 94, 2108-2122.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Mills, J. H. (1973a). Temporary and permanent threshold shifts produced by nine-day exposures to noise. J. Speech Hear. Res. 16, 46-438.

Mills, J. H. (1973b). Threshold shifts produced by exposure to noise in chinchillas with noise-induced hearing losses. J. Speech Hear. Res. 16, 700-708.

Mills, J. H. (1976). Threshold shifts produced by a 90-day exposure to noise. In: D. Henderson, R. P. Hamernik, D. S. Dosanjh, and J. H. Mills (Eds.), Effects of Noise on Hearing, Raven Press, New York, pp. 265-275.

Mills, J. H. (1992). Noise induced hearing loss: Effects of age and existing hearing loss. In: A. Dancer, D. Henderson, R. J. Salvi, R. P. Hamernik (Eds.), Noise-Induced Hearing Loss, Mosby Year Book, St. Louis, MO, pp. 237-245.

Mitchell, C., Brummett, R. E., and Vernon, J. A. (1977). Frequency effects of temporary N1 depression following acoustic overload. Arch. Otolaryngol. 103, 117-123.

Miyakita, T., Hellström, P.-A., Frimanson, E., and Axelsson, A. (1992). Effect of low level acoustic stimulation on temporary threshold shift in young humans. Hear. Res. 60, 149-155.

Moody, D. B., Stebbins, W. C., Johnsson, L. -G., and Hawkins, J. E., Jr. (1976). Noise-induced hearing loss in the monkey. In: D. Henderson, R. P. Hamernik, D. S. Dosanjh, and J. H. Mills (Eds.), Effects of Noise on Hearing, Raven Press, New York, pp. 309-325.

Mountain, D. C. (1980). Changes in endolymphatic potential and crossed olivocochlear bundle stimulation alter cochlear mechanics. Science 210, 71-72.

Myers, M. W., Quirk, W. S., Rizk, S. S., Miller, J. M., and Altschuler, R. A. (1992). Expression of the major mammalian stress protein in the rat cochlea following transient ischemia. Laryngoscope 102, 981-987.

National Institutes of Health (Revised, 1985). NIH Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23). Washington, D.C.: U.S. Government Printing Office.

Neely, J. G., Thompson, A. M., Gower, D. J. (1991). Detection and localization of heat shock protein in the normal guinea pig cochlea. Hear. Res. 52, 403-406.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Norton, S. J., and Rubel, E. W. (1990). Active and passive ADP components in mammalian and avian ears. In: P. Dallos, C. D. Geisler, J. W. Matthews, M. A. Ruggero, and C. R. Steele (Eds.), The Mechanics and Biophysics of Hearing, Springer-Verlag, Berlin, pp. 219-225.

Oberholtzer, J. C., Baettger, C., Summers, M. C., and Matschinsky, F. M. (1988). The 28 kDa calbindin is a major calcium binding protein in the basilar papilla of the chick. Proc. Natl. Acad. Sci. USA 85, 3387-3390.

Passchier-Vermeer, W. (1974). Hearing loss due to continuous exposure to steady-state broad band noise. J. Acoust. Soc. Am. 56, 1585-1593.

Prince, M. M., and Matanoski, G. M. (1991). Problems on ascertaining the combined effects of exposure: Results of an occupational cohort study of the joint effects of noise and smoking on hearing acuity. In: L. Fletcher (Ed.), Proceedings of the IVth International Conference of the Combined Effects of Environmental Factors, Johns Hopkins University, Baltimore, MD, pp. 87-91.

Puel, J. -L., Bobbin, R. P., and Fallon, M. (1988a). The active process is affected first by intense sound exposure. Hear. Res. 37, 53-64.

Puel, J. -L., Bobbin, R. P., and Fallon, M. (1988b). An ipsilateral cochlear efferent loop protects the cochlea during intense sound exposure. Hear. Res. 37, 65-70.

Puel, J. -L., Durrieu, J. Ph., Rebillard, G., Vidal, D., Assié, R., and Uziel, A. (1995). Comparison between auditory brainstem response and distortion products otoacoustic emissions after temporary threshold shift in guinea pig. Acta Acustica 3, 75-82.

Rajan, R. (1992). Protective functions of the efferent pathways to the mammalian cochlea: A review. In: A. Dancer, D. Henderson, R. J. Salvi, R. P. Hamernik (Eds.), Noise-Induced Hearing Loss, Mosby Year Book, St. Louis, MO, pp. 429-444.

Rajan, R. (1996). Efferent and priming modulation of noise-induced hearing loss. In: A. Axelsson, H. M. Borchgrevink, R. P. Hamernik, P. -A. Hellström, D. Henderson, and R. J. Salvi (Eds.), Scientific Basis of Noise-Induced Hearing Loss, Thieme Medical Publishers, Inc., New York, pp. 159-171.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Rajan, R. and Johnstone, B. M. (1983). Cross cochlear influences on monaural temporary threshold shifts. Hear. Res. 9, 279-294.

Roberto, M., Hamernik, R. P., Salvi, R. J., Henderson, D., and R. Milone (1985). Impact noise and the equal energy hypothesis. J. Acoust. Soc. Am. 77, 1514-1520.

Rodriguez, G. P., and Gerhardt, K. J. (1988). Adaptation properties of the acoustic reflex in response to continuous-, intermittent- and industrial-noise stimulation. Audiology 27, 344-355.

Rosowski, J. J., Peake, W. T., and White, J. R. (1984). Cochlear nonlinearities inferred from two-tone distortion products in the ear canal of the alligator lizard. Hear. Res. 18, 141-158.

Ryan, A. F., Bennett, T. M., Woolf, N. K., and Axelsson, A. (1994). Protection from noise-induced hearing loss by prior exposure to a nontraumatic stimulus: Role of the middle ear muscles. Hear. Res. 72, 23-28.

Salvi, R., Perry, J. Hamernik, R. P., and Henderson, D. (1982). Relationship between cochlear pathologies and auditory nerve and behavioral responses following acoustic trauma. In: R. P. Hamernik, D. Henderson, and R. Salvi (Eds.), New Perspectives on Noise-induced Hearing Loss, Raven Press, New York, pp. 165-188.

Saunders, J. C., Cohen, Y. E., and Szymko, Y. M. (1991). The structural and functional consequences of acoustic injury in the cochlea and peripheral auditory system: A five year update. J. Acoust. Soc. Am. 90, 136-146.

Saunders, J. C., Dear, S. P., and Schneider, M. E. (1985). The anatomical consequences of acoustic injury: A review and tutorial. J. Acoust. Soc. Am. 78, 833-860.

Schmiedt, R. A., and Adams, J. C. (1981). Stimulated acoustic emissions in the ear canal of the gerbil. Hear. Res. 5, 295-305.

Siegel, J. H., and Kim, D. O. (1982). Cochlear biomechanics: Vulnerability to acoustic trauma and other alterations as seen in neural responses and ear-canal sound pressure. In: R. P. Hamernik, D. Henderson, and R. Salvi (Eds.), New Perspectives on Noise-Induced Hearing Loss, Raven Press, New York, pp. 137-151.

Siegel, J. H., Kim, D. O., and Molnar, C. E. (1982). Effects of altering Organ of Corti on cochlear

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

distortion products $f_2$-$f_1$ and $2f_1$-$f_2$. J. Neurophysiol. 47, 303-328.

Sinex, D. G., Clark, W. W., and Bohne, B. A. (1987). Effects of periodic rest on physiological measures of auditory sensitivity following exposure to noise. J. Acoust. Soc. Am. 82(4), 1265-1273.

Skellett, R. A., Crist, J. R., Fallon, M., and Bobbin, R. P. (in press). Chronic low-level noise exposure alters distortion product otoacoustic emissions. Hear. Res.

Slepecky, N., Hamernik, R., Henderson, D., and Coling, D. (1982). Correlation of audiometric data with changes in cochlear with changes in cochlear hair cell stereocilia resulting from impulse noise trauma. Acta Otolaryngol. 93, 329-340.

Smoorenburg, G. F. (1972). Combination tones and their origin. J. Acoust. Soc. Am. 52, 615-632.

Subramaniam, M., Campo, P., and Henderson, D. (1991a). The effect of exposure level on the development of progressive resistance to noise. Hear. Res. 52, 181-188.

Subramaniam, M., Campo, P., and Henderson, D. (1991b). Development of resistance to hearing loss from high frequency noise. Hear. Res. 56, 65-68.

Subramaniam, M., Henderson, D., Campo, P., and Spongr, V. P. (1992). The effect of "conditioning" on hearing loss from a high frequency traumatic exposure. Hear. Res. 58, 57-62.

Subramaniam, M., Henderson, D., and Spongr, V. P. (1993a). Protection from noise induced hearing loss: Is prolonged "conditioning" necessary? Hear. Res. 65, 234-239.

Subramaniam, M., Henderson, D., and Spongr, V. P. (1993b). Effect of low-frequency "conditioning" on hearing loss from high-frequency exposure. J. Acoust. Soc. Am. 93, 952-956.

Subramaniam, M., Henderson, D., and Spongr, V. (1994a). The relationship among distortion-product otoacoustic emissions, evoked potential thresholds, and outer hair cells following interrupted noise exposures. Ear and Hear. 15, 299-309.

Subramaniam, M., Henselman, L. W., Spongr, V., Henderson, D., and Powers, N. L. (1995). Effect of high-frequency interrupted noise exposures on evoked-

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

potential thresholds, distortion-product otoacoustic emissions, and outer hair cell loss. Ear and Hear. 16, 372-381.

Subramaniam, M., Salvi, R. J., Spongr, V. P., Henderson, D., and Powers, N. L. (1994b). Changes in distortion product otoacoustic emissions and outer hair cells following interrupted noise exposures. Hear. Res. 74, 204-216.

Sulkowski, W. J., Kowalska, S., and Lipowczan, A. (1983). Hearing loss in weavers and drop-forge hammermen: Comparative study of the effects of steady-state and impulse noise. In: G. Rossi (Ed.), Proceedings of the Fourth International Congress on Noise as a Public Health Problem, Vol. 1, Milan, Italy.

Sulkowski, W. J., Lipowczan, A., and Latkowski, B. (1980). Field study on effects of industrial impulse noise upon permanent threshold shift. In: J. V. Tobias, G. Jansen, and W. D. Ward (Eds.), Proceedings of the Third International Congress on Noise as a Public Health Problem (Am. Speech Lang. Hear. Assoc., ASHA Rep. 10, Rockville, MD).

Syka, J., and Popelar, J. (1980). Hearing threshold shifts from prolonged exposure to noise in guinea pigs. Hear. Res. 3, 205-213.

Szanto, C., and Ionescu, M. (1983). Influence of age and sex on hearing threshold levels in workers exposed to different intensity levels of occupational noise. Audiol. 22, 339-356.

Taylor, W., Lempert, B., Pelmear, P., Hemstock, I., and Kershaw, J. (1984). Noise levels and hearing thresholds in the drop forging industry. J. Acoust. Soc. Am. 76, 807-819.

Taylor, W., and Pelmear, P. L. (1976). Noise levels and hearing thresholds in the drop forging industry. Med. Res. Council Project Rep., Grant G972/784/C, June, London.

Thompson, A. M., and Neely, J. G. (1992). Induction of heat shock proteins in interdental cells by hyperthermia. Otolaryngol. Head Neck Surg. 107, 769-774.

U.S. Air Force (1956). Hazardous noise exposure. Air Force Regulation 106-163, Washington, DC, USAF.

Voigt, P., Godenhielm, B., and Ostland, E. (1980). Impulse noise-measurement and assessment of the risk of noise

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

induced hearing loss. Scand. Audiol. Suppl. 12, 319-325.

Ward, W. D. (1970). Temporary threshold shift and damage-risk criteria for intermittent noise exposures. J. Acoust. Soc. Am. 48, 561-574.

Ward, W. D. (1976). A comparison of the effects of continuous, intermittent, and impulse noise. In: D. Henderson, R. P. Hamernik, D. S. Dosanjh, and J. H. Mills (Eds.), Effects of Noise on Hearing, Raven Press, New York, pp. 407-420.

Ward, W. D., and Duvall, A. J. (1971). Behavioral and ultrastructural correlates of acoustic trauma. Ann. Otol. Rhinol. Laryngol. 80, 881-896.

Ward, W. D., Santi, P. A., Duvall, A. J., and Turner, C. W. (1981). Total energy and critical intensity concepts in noise damage. Ann. Otol. Rhinol. Laryngol. 90, 584-590.

Welch, W. J. (1992). Mammalian stress response: Cell physiology, structure/function of stress proteins and implications for medicine and disease. Physiol. Rev. 72, 1063-1080.

White, D. R., Boettcher, F. A., and Holley, B. L. (1996). Effectiveness of intermittent and continuous acoustic stimulation in preventing noise-induced hearing loss. In: G. R. Popelka, Ph.D. (Ed.), Abstracts of the Nineteenth Midwinter Research Meeting, Association for Research in Otolaryngology, St. Petersburg Beach, Florida, p. 34.

Whitehead, M. L., Lonsbury-Martin, B. L., and Martin, G. K. (1992a). Evidence for two discrete sources of $2f_1$-$f_2$ distortion-product otoacoustic emissions in the rabbit: I. Differential dependence on stimulus parameters. J. Acoust. Soc. Am. 91, 1587-1607.

Whitehead, M. L., Lonsbury-Martin, B. L., and Martin, G. K. (1992b). Evidence for two discrete sources of $2f_1$-$f_2$ distortion-product otoacoustic emissions in the rabbit: II. Differential physiological vulnerability. J. Acoust. Soc. Am. 92, 2662-2682.

Wilson, J. P. (1980). The combination tones, $2f_1$-$f_2$, in psychophysics and ear-canal recording. In: G. Van Den Brink and F. A. Bilson (Eds.), Psychophysical, Physiological, and Behavioral Studies in Hearing, Delft U. P., Delft, The Netherlands, pp. 43-50.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Zakrisson, J. -E., Borg, E., Lidén, G., and Nilsson, R. (1980). Stapedius reflex in industrial impact noise: Fatigability and role for temporary threshold shift (TTS). Scand. Audiol. Suppl. 12, 326-334.

Zurek, P. M., Clark, W. W., and Kim, D. O. (1982). The behavior of acoustic distortion products in the ear canals of chinchillas with normal and damaged ears. J. Acoust. Soc. Am. 72, 774-780.

Zwicker, E. (1986). Suppression and $(2f_1-f_2)$-difference tones: A nonlinear cochlear preprocessing model with active feedback. J. Acoust. Soc. Am. 80, 163-176.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

## APPENDIX A

## INDIVIDUAL ANIMAL DPOAE AMPLITUDE DATA

The DPOAE amplitude data from each individual animal is represented in tabular form for each exposure group according to the frequency of $f_2$. Within each set of data shown on the following pages, the first column of values represents the intenstiy level of the primary tones (20-70 dB SPL) used to elicit the DPOAE responses. The remaining columns contain the corresponding DPOAE amplitudes (in dB SPL) for each animal (Animal #) within the given exposure group.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=707 Hz

Aged Normal Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2475 |
| 20 | -6.33 | -6.98 | -6.54 | -7.35 | -7.20 | -7.35 | -7.66 | -7.67 | -6.31 | -6.64 | -7.62 | -7.99 | -7.25 | -7.89 |
| 25 | -7.43 | -6.73 | -5.79 | -7.53 | -6.88 | -7.62 | -6.87 | -7.36 | -6.09 | -6.66 | -7.54 | -7.08 | -7.52 | -6.21 |
| 30 | -6.91 | -6.92 | -5.48 | -5.86 | -6.54 | -6.61 | -7.15 | -6.62 | -3.80 | -6.26 | -7.41 | -6.76 | -6.31 | -7.46 |
| 35 | -4.95 | -5.38 | -4.06 | -6.38 | -6.66 | -4.25 | -4.11 | -7.62 | -1.01 | -6.11 | -6.62 | -6.00 | -7.23 | -7.13 |
| 40 | -2.54 | -2.01 | -0.94 | -1.73 | -4.03 | -1.76 | 1.04 | -5.93 | 2.93 | -0.37 | 0.35 | -1.67 | -0.72 | -5.46 |
| 45 | 5.28 | 2.59 | 3.22 | 1.93 | -0.59 | 2.12 | 6.69 | 2.06 | 5.64 | 5.33 | 4.77 | 4.75 | 3.98 | -5.32 |
| 50 | 9.26 | 3.80 | 5.88 | 2.15 | -0.72 | 3.43 | 7.44 | 6.25 | 4.89 | 8.45 | 6.20 | 9.75 | 5.30 | -4.68 |
| 55 | 6.61 | 9.30 | 5.10 | 0.59 | 8.05 | 4.47 | 1.17 | 5.66 | 4.58 | 3.57 | 11.20 | 11.53 | 3.18 | -2.52 |
| 60 | 10.86 | 17.53 | 16.72 | 17.47 | 20.34 | 16.13 | 19.60 | 14.01 | 21.26 | 18.42 | 21.65 | 2.29 | 16.67 | 7.83 |
| 65 | 26.87 | 25.44 | 26.79 | 25.79 | 28.53 | 25.19 | 28.19 | 27.47 | 27.58 | 28.22 | 29.68 | 23.43 | 27.00 | 18.36 |
| 70 | 32.36 | 31.85 | 32.28 | 33.05 | 30.10 | 33.53 | 33.43 | 33.78 | 32.08 | 32.63 | 33.40 | 33.97 | 28.98 | 24.89 |

Interrupted Conditioning Group (n=14)

| | Animal # | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
| 20 | -7.27 | -6.78 | -7.12 | -6.72 | -6.03 | -7.64 | -6.57 | -6.73 | -6.18 | -6.02 | -7.54 | -6.70 | -7.28 | -7.51 |
| 25 | -7.43 | -6.53 | -6.23 | -6.65 | -6.74 | -7.52 | -6.16 | -6.62 | -5.87 | -7.18 | -6.73 | -6.93 | -7.72 | -7.63 |
| 30 | -5.63 | -6.49 | -5.71 | -7.71 | -5.92 | -7.15 | -6.92 | -6.97 | -7.03 | -6.20 | -6.88 | -5.85 | -7.87 | -7.15 |
| 35 | -5.49 | -6.47 | -5.85 | -6.85 | -5.07 | -5.04 | -7.24 | -6.02 | -6.17 | -5.80 | -3.24 | -5.71 | -6.89 | -7.85 |
| 40 | -4.12 | -3.78 | -0.79 | -1.44 | -2.76 | -2.20 | -2.88 | -1.53 | -6.63 | -2.45 | 2.98 | -3.45 | 0.56 | -4.55 |
| 45 | 0.70 | 3.80 | 6.18 | 5.18 | 0.20 | 2.41 | 1.62 | 3.52 | 2.11 | 0.70 | 6.62 | -0.54 | 5.69 | 0.20 |
| 50 | 6.47 | 10.80 | 11.11 | 10.58 | 4.95 | 8.58 | 8.13 | 7.35 | 9.58 | 3.67 | 11.57 | 0.80 | 9.22 | 4.62 |
| 55 | 11.50 | 16.87 | 15.02 | 14.03 | 8.01 | 13.30 | 12.19 | 9.44 | 15.53 | 10.28 | 14.90 | 3.76 | 10.92 | 8.07 |
| 60 | 11.23 | 20.46 | 14.91 | 14.47 | 3.61 | 16.44 | 14.32 | 10.13 | 19.13 | 13.49 | 17.85 | 11.67 | 16.63 | 1.86 |
| 65 | 14.03 | 20.59 | 15.21 | 22.41 | 22.00 | 22.13 | 20.75 | 22.16 | 22.21 | 21.12 | 23.52 | 23.79 | 22.55 | 21.11 |
| 70 | 29.73 | 20.33 | 30.02 | 23.80 | 31.21 | 28.72 | 28.83 | 27.40 | 23.04 | 26.80 | 26.41 | 27.69 | 15.44 | 28.29 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=707 Hz

Continuous Conditioning Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
| 20 | -7.77 | -6.45 | -7.46 | -7.46 | -6.46 | -6.81 | -6.33 | -6.42 | -5.95 | -6.73 | -6.63 | -7.79 | -6.93 | -6.63 |
| 25 | -6.23 | -6.78 | -6.56 | -6.98 | -5.93 | -7.58 | -7.12 | -7.18 | -6.77 | -7.28 | -6.27 | -6.98 | -6.86 | -7.17 |
| 30 | -6.57 | -7.33 | -7.97 | -7.10 | -6.79 | -7.23 | -6.84 | -6.19 | -6.02 | -6.67 | -7.11 | -6.44 | -7.82 | -7.37 |
| 35 | -6.54 | -7.01 | -7.57 | -6.15 | -5.76 | -6.31 | -7.94 | -6.26 | -7.70 | -6.24 | -6.57 | -6.87 | -7.27 | -7.32 |
| 40 | -7.21 | -6.89 | -7.53 | -6.06 | -7.14 | -6.93 | -6.60 | -6.43 | -6.29 | -5.85 | -5.72 | -6.62 | -7.11 | -6.51 |
| 45 | -6.38 | -5.78 | -2.72 | -5.24 | -5.85 | -2.99 | -2.45 | -3.39 | -5.16 | -2.47 | -3.25 | -5.19 | -5.75 | -6.74 |
| 50 | -2.73 | 4.92 | 3.12 | -0.48 | -0.85 | 1.93 | 4.37 | -0.62 | -1.43 | 0.63 | 1.01 | -1.13 | -1.84 | -2.83 |
| 55 | 2.95 | 7.20 | 9.22 | 1.75 | 5.44 | 8.05 | 9.00 | 1.36 | 1.82 | 7.19 | 4.40 | 2.20 | 0.08 | -1.09 |
| 60 | 6.20 | 9.48 | 10.89 | 7.01 | 11.64 | 10.07 | 11.41 | 11.28 | 4.53 | 10.83 | 5.25 | 6.91 | 7.54 | 3.93 |
| 65 | 19.08 | 20.20 | 20.30 | 20.32 | 21.00 | 20.87 | 17.86 | 21.59 | 19.40 | 19.46 | 20.08 | 20.47 | 19.97 | 16.58 |
| 70 | 25.26 | 25.22 | 28.81 | 25.96 | 24.15 | 27.74 | 28.30 | 31.02 | 30.55 | 26.33 | 30.02 | 28.92 | 24.59 | 30.34 |

Blast Only Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
| 20 | -6.85 | -6.71 | -7.15 | -7.01 | -6.77 | -6.88 | -6.82 | -7.48 | -6.84 | -6.63 | -7.97 | -7.46 | -6.43 | -7.56 |
| 25 | -5.87 | -7.15 | -6.33 | -6.57 | -6.10 | -7.10 | -6.45 | -6.51 | -6.56 | -6.77 | -6.66 | -6.64 | -7.68 | -6.88 |
| 30 | -5.74 | -7.89 | -7.20 | -7.73 | -6.33 | -6.83 | -6.29 | -7.11 | -7.17 | -6.33 | -7.94 | -7.57 | -7.60 | -6.72 |
| 35 | -6.39 | -6.65 | -6.73 | -7.17 | -7.66 | -6.57 | -5.62 | -7.67 | -6.85 | -5.74 | -7.62 | -7.51 | -7.02 | -7.12 |
| 40 | -5.81 | -4.82 | -5.84 | -6.63 | -5.35 | -5.80 | -7.15 | -6.06 | -6.24 | -4.97 | -7.64 | -6.23 | -5.70 | -6.10 |
| 45 | -7.93 | -4.05 | -0.96 | -5.05 | -2.44 | 3.10 | -4.27 | -2.59 | -4.12 | 0.56 | -6.13 | 0.59 | -6.90 | -6.84 |
| 50 | -3.62 | 1.27 | 6.36 | -0.39 | 3.40 | 9.00 | -0.90 | 2.60 | 0.84 | 5.43 | -2.57 | 6.15 | -2.26 | -0.98 |
| 55 | 2.92 | 6.38 | 11.88 | 8.57 | 10.87 | 15.27 | 2.13 | 10.24 | 2.38 | 8.26 | 1.44 | 12.10 | -0.63 | 6.13 |
| 60 | 10.37 | 11.29 | 18.71 | 17.35 | 18.59 | 21.51 | 3.17 | 16.53 | 12.37 | 11.16 | 5.58 | 17.11 | 7.05 | 12.86 |
| 65 | 14.66 | 18.70 | 22.75 | 21.13 | 23.45 | 26.58 | 14.19 | 20.50 | 20.52 | 21.43 | 17.37 | 22.17 | 18.97 | 18.96 |
| 70 | 10.25 | 20.22 | 19.77 | 21.32 | 21.08 | 24.77 | 15.03 | 23.41 | 16.43 | 21.07 | 21.82 | 22.11 | 16.17 | 21.82 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=707 Hz

Interrupted Conditioning then Blast Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2642 | 2644 | 2654 | 2655 | 2656 | 2657 | 2659 | 2660 | 2662 | 2664 | 2665 | 2683 | 2684 | 2685 |
| 20 | -7.63 | -7.24 | -7.68 | -7.31 | -7.25 | -6.83 | -7.49 | -7.54 | -7.32 | -7.66 | -7.04 | -6.76 | -7.84 | -6.77 |
| 25 | -6.32 | -7.51 | -7.71 | -6.76 | -6.85 | -7.03 | -6.83 | -6.39 | -6.48 | -7.54 | -6.43 | -7.12 | -6.23 | -7.38 |
| 30 | -6.41 | -7.13 | -7.35 | -7.21 | -7.38 | -6.78 | -6.38 | -7.27 | -6.32 | -7.38 | -6.40 | -7.24 | -7.22 | -6.43 |
| 35 | -7.10 | -6.01 | -7.51 | -7.57 | -7.59 | -6.87 | -6.35 | -6.49 | -6.10 | -7.71 | -6.98 | -7.18 | -6.54 | -5.94 |
| 40 | -6.71 | -6.84 | -7.77 | -6.84 | -7.40 | -7.31 | -6.29 | -5.95 | -5.39 | -7.09 | -6.56 | -6.32 | -5.66 | -6.71 |
| 45 | -2.45 | -6.35 | -7.40 | -4.77 | 1.36 | -5.12 | -6.66 | -6.32 | -4.12 | -6.66 | -6.46 | -2.05 | -1.60 | -4.03 |
| 50 | 3.41 | -6.24 | -3.32 | -0.14 | 7.02 | -1.34 | -6.05 | -6.85 | 0.95 | -1.00 | -3.43 | 5.91 | 3.14 | 1.07 |
| 55 | 7.64 | -1.29 | 6.74 | 2.43 | 9.69 | 3.34 | -4.98 | 0.68 | 4.92 | 5.50 | -1.90 | 12.44 | 7.48 | 7.05 |
| 60 | 12.75 | 1.21 | 16.08 | 4.41 | 7.05 | 8.53 | 0.39 | 7.17 | 11.13 | 12.40 | 5.45 | 18.70 | 12.70 | 13.18 |
| 65 | 19.21 | 5.29 | 22.94 | 19.02 | 18.37 | 11.39 | 3.21 | 12.57 | 20.19 | 14.12 | 19.30 | 23.89 | 21.16 | 12.58 |
| 70 | 24.17 | 7.72 | 26.13 | 15.17 | 18.33 | 14.67 | 7.97 | 16.31 | 22.91 | 8.13 | 22.22 | 24.95 | 19.25 | 20.38 |

Continuous Conditioning then Blast Group (n=14)

| dB | 2594 | 2595 | 2596 | 2597 | 2598 | 2599 | 2606 | 2607 | 2608 | 2609 | 2610 | 2611 | 2612 | 2613 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -6.82 | -5.17 | -6.99 | -6.30 | -7.07 | -8.14 | -7.49 | -6.37 | -7.18 | -7.63 | -7.54 | -6.98 | -7.15 | -6.27 |
| 25 | -6.32 | -5.74 | -5.12 | -7.02 | -6.21 | -7.71 | -7.96 | -5.85 | -6.54 | -6.57 | -7.26 | -6.32 | -7.32 | -6.08 |
| 30 | -6.15 | -5.09 | -7.49 | -1.78 | -5.23 | -8.23 | -6.90 | -6.35 | -7.02 | -7.13 | -7.34 | -5.85 | -7.12 | -7.01 |
| 35 | -7.63 | -5.29 | -6.19 | -4.15 | -5.40 | -8.01 | -7.66 | -6.66 | -4.73 | -7.90 | -6.95 | -5.68 | -6.21 | -6.92 |
| 40 | -6.11 | -4.78 | -5.54 | -2.89 | -6.12 | -7.48 | -6.90 | -5.87 | -5.71 | -5.58 | -7.64 | -6.73 | -4.98 | -5.83 |
| 45 | -2.98 | -4.78 | -2.23 | 2.86 | -5.52 | -4.56 | -2.48 | -4.55 | -4.84 | -7.20 | -5.82 | -5.07 | -3.48 | 0.41 |
| 50 | 3.70 | 2.08 | 3.43 | 7.02 | 2.38 | 3.52 | 4.84 | -2.28 | -4.19 | -2.15 | 0.28 | -2.84 | 0.48 | 5.97 |
| 55 | 11.11 | 8.75 | 8.34 | 11.16 | 6.97 | 7.97 | 9.90 | 5.67 | 2.57 | 1.71 | 2.93 | 4.92 | 6.51 | 10.36 |
| 60 | 17.66 | 15.24 | 11.86 | 16.18 | 11.72 | 12.36 | 12.88 | 14.05 | 6.36 | 9.60 | 4.37 | 11.25 | 10.75 | 10.38 |
| 65 | 22.97 | 17.47 | 19.56 | 21.54 | 15.98 | 17.65 | 16.70 | 16.64 | 9.47 | 15.28 | 10.98 | 15.71 | 15.31 | 6.38 |
| 70 | 21.63 | 20.30 | 14.17 | 20.27 | 9.15 | 19.50 | 7.39 | 8.03 | 15.35 | 11.50 | 9.73 | 6.20 | 16.72 | 22.66 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=1000 Hz

Aged Normal Group (n=14)

Animal #

| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -10.21 | -8.57 | -8.54 | -9.96 | -9.21 | -10.21 | -9.80 | -10.64 | -9.33 | -8.68 | -9.17 | -10.49 | -9.88 | -9.34 |
| 25 | -10.10 | -9.05 | -7.35 | -10.81 | -9.50 | -10.87 | -9.49 | -10.10 | -8.75 | -9.34 | -8.84 | -9.87 | -9.49 | -10.96 |
| 30 | -10.09 | -7.97 | -7.86 | -10.58 | -9.36 | -10.98 | -9.70 | -10.59 | -8.41 | -9.99 | -10.27 | -11.01 | -10.04 | -9.33 |
| 35 | -10.87 | -9.25 | -7.49 | -10.20 | -8.00 | -7.06 | -7.60 | -9.75 | -6.71 | -5.48 | -9.14 | -7.82 | -8.73 | -7.78 |
| 40 | -6.96 | -4.68 | -3.17 | -3.79 | -3.24 | -2.24 | -2.01 | -9.95 | -3.99 | -0.26 | -8.67 | -3.95 | -5.21 | -8.24 |
| 45 | 1.53 | 0.12 | 1.37 | 0.57 | 0.04 | 1.61 | 1.50 | -2.70 | 1.02 | 6.13 | -2.69 | 5.74 | -3.81 | -5.55 |
| 50 | 6.58 | 3.58 | 3.80 | 3.71 | 2.71 | 2.93 | 2.52 | 1.37 | 3.73 | 7.58 | 1.87 | 10.64 | 0.46 | -2.14 |
| 55 | 5.15 | 2.09 | 1.25 | 1.14 | 1.21 | -3.25 | 2.90 | -1.76 | -2.81 | 5.08 | 1.58 | 12.63 | -0.85 | 2.80 |
| 60 | 8.19 | 7.40 | 12.05 | 7.22 | 12.48 | 9.44 | 18.07 | 12.15 | 16.61 | 16.63 | 7.56 | 17.88 | 6.13 | -6.62 |
| 65 | 23.27 | 22.92 | 22.95 | 23.19 | 24.70 | 23.55 | 26.41 | 25.33 | 25.85 | 25.63 | 22.15 | 27.56 | 16.82 | 13.07 |
| 70 | 30.03 | 30.08 | 26.72 | 31.12 | 28.31 | 31.11 | 30.36 | 30.38 | 28.77 | 29.80 | 32.14 | 32.79 | 24.40 | 22.41 |

Interrupted Conditioning Group (n=14)

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -9.13 | -8.59 | -8.96 | -9.76 | -9.32 | -9.84 | -8.50 | -8.84 | -9.15 | -9.18 | -9.32 | -9.56 | -9.87 | -10.26 |
| 25 | -8.73 | -8.81 | -7.67 | -9.59 | -9.82 | -8.68 | -8.51 | -9.20 | -9.08 | -9.49 | -10.23 | -9.51 | -10.75 | -9.46 |
| 30 | -8.65 | -8.87 | -9.87 | -9.43 | -9.45 | -10.23 | -9.66 | -8.18 | -8.67 | -8.31 | -9.57 | -9.35 | -9.96 | -10.55 |
| 35 | -8.24 | -8.21 | -7.42 | -9.71 | -6.32 | -9.95 | -8.42 | -7.88 | -9.96 | -8.56 | -8.87 | -7.29 | -10.90 | -9.82 |
| 40 | -8.70 | -9.04 | -4.16 | -9.02 | -3.84 | -9.30 | -7.78 | -4.98 | -9.53 | -3.89 | -3.36 | -4.40 | -10.53 | -6.11 |
| 45 | 0.17 | -6.46 | 1.30 | -4.59 | 1.60 | -2.52 | -3.76 | 1.83 | -4.77 | 2.30 | 1.47 | 1.68 | -8.65 | 0.86 |
| 50 | 9.98 | 3.02 | 8.49 | 3.96 | 7.91 | 2.85 | 4.07 | 8.30 | 1.63 | 7.55 | 8.20 | 7.53 | -6.65 | 7.59 |
| 55 | 14.24 | 11.72 | 14.27 | 10.14 | 13.05 | 7.36 | 11.01 | 13.82 | 9.15 | 11.80 | 13.56 | 11.73 | 3.20 | 13.41 |
| 60 | 17.46 | 18.00 | 17.34 | 13.83 | 15.71 | 12.37 | 15.86 | 16.74 | 15.10 | 13.93 | 17.27 | 12.24 | 13.05 | 17.14 |
| 65 | 18.46 | 20.84 | 18.13 | 17.02 | 15.43 | 17.50 | 16.71 | 17.82 | 20.54 | 16.17 | 19.12 | 11.35 | 19.37 | 19.35 |
| 70 | 22.01 | 24.44 | 15.59 | 21.04 | 21.97 | 18.98 | 19.56 | 15.04 | 24.08 | 21.80 | 25.19 | 17.28 | 28.62 | 18.79 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=1000 Hz

**Continuous Conditioning Group (n=14)**

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **dB** | **2676** | **2677** | **2678** | **2679** | **2680** | **2681** | **2682** | **2686** | **2687** | **2688** | **2689** | **2690** | **2691** | **2692** |
| **20** | -10.24 | -9.00 | -9.20 | -10.04 | -10.07 | -10.53 | -10.07 | -10.29 | -9.45 | -10.74 | -8.78 | -8.95 | -10.47 | -10.20 |
| **25** | -10.07 | -9.26 | -10.03 | -10.31 | -9.28 | -9.07 | -9.45 | -9.85 | -8.87 | -11.20 | -9.42 | -9.59 | -10.04 | -10.14 |
| **30** | -9.88 | -9.54 | -10.53 | -9.48 | -10.05 | -10.32 | -10.06 | -10.05 | -9.54 | -9.54 | -9.88 | -9.91 | -9.09 | -9.78 |
| **35** | -9.14 | -10.29 | -10.30 | -10.61 | -10.07 | -10.43 | -10.18 | -10.31 | -8.76 | -9.65 | -9.66 | -10.04 | -9.92 | -9.64 |
| **40** | -10.53 | -9.82 | -10.24 | -9.93 | -9.79 | -10.40 | -9.48 | -10.16 | -9.67 | -9.77 | -8.52 | -9.57 | -10.42 | -10.06 |
| **45** | -8.33 | -8.06 | -9.58 | -9.57 | -9.49 | -7.74 | -6.37 | -7.76 | -7.99 | -7.74 | -9.73 | -8.02 | -9.20 | -9.89 |
| **50** | -7.96 | -2.70 | -4.94 | -4.06 | -6.81 | -5.30 | -0.37 | -1.73 | -2.96 | -3.36 | -4.39 | -1.06 | -4.45 | -6.31 |
| **55** | -0.82 | 4.46 | 4.64 | 3.90 | 0.55 | 4.01 | 8.92 | 6.58 | 5.18 | 4.83 | 4.34 | 6.36 | 2.29 | 3.22 |
| **60** | 6.46 | 11.58 | 12.20 | 10.17 | 7.31 | 11.98 | 14.85 | 13.52 | 11.90 | 12.41 | 12.55 | 12.03 | 10.38 | 10.70 |
| **65** | 13.73 | 15.97 | 18.19 | 16.57 | 11.28 | 16.76 | 16.24 | 20.93 | 17.25 | 18.45 | 19.75 | 16.40 | 13.45 | 19.80 |
| **70** | 17.80 | 20.11 | 24.15 | 21.21 | 16.34 | 22.36 | 22.32 | 25.71 | 23.91 | 22.83 | 24.46 | 23.19 | 21.18 | 26.08 |

**Blast Only Group (n=14)**

| **dB** | **2600** | **2601** | **2614** | **2615** | **2616** | **2617** | **2618** | **2619** | **2620** | **2648** | **2658** | **2661** | **2663** | **2666** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **20** | -9.59 | -8.53 | -10.62 | -9.28 | -10.72 | -8.96 | -9.63 | -10.75 | -9.32 | -10.65 | -9.90 | -10.86 | -10.23 | -10.15 |
| **25** | -9.54 | -9.59 | -12.45 | -8.06 | -10.59 | -9.52 | -8.90 | -10.02 | -9.71 | -10.12 | -9.78 | -10.47 | -9.39 | -9.46 |
| **30** | -9.96 | -8.69 | -9.81 | -10.04 | -9.86 | -8.04 | -8.52 | -9.45 | -9.71 | -9.86 | -10.57 | -9.51 | -10.09 | -9.82 |
| **35** | -7.51 | -8.85 | -10.56 | -8.92 | -10.03 | -9.40 | -8.49 | -9.90 | -9.49 | -9.46 | -9.99 | -9.05 | -8.60 | -9.52 |
| **40** | -9.24 | -9.62 | -10.09 | -9.29 | -10.60 | -8.58 | -9.63 | -9.21 | -9.37 | -8.16 | -9.99 | -8.85 | -9.82 | -9.93 |
| **45** | -6.96 | -7.27 | -9.53 | -8.40 | -9.62 | -7.40 | -9.91 | -10.15 | -5.87 | -9.10 | -9.57 | -9.76 | -8.12 | -9.07 |
| **50** | -4.60 | -7.49 | -4.50 | -4.89 | -9.10 | -2.08 | -6.04 | -4.96 | -1.51 | -7.26 | -9.30 | -6.94 | -8.40 | -7.87 |
| **55** | 0.25 | -1.64 | 4.53 | 2.86 | -2.90 | 5.36 | -0.60 | 3.76 | 5.45 | -4.77 | -8.01 | -3.17 | -2.20 | -0.84 |
| **60** | 1.04 | 1.04 | 12.69 | 10.16 | 5.80 | 12.28 | 5.69 | 11.15 | 11.80 | 1.43 | 1.38 | -0.60 | 5.79 | 5.55 |
| **65** | 0.47 | -2.09 | 18.24 | 13.22 | 12.80 | 17.19 | 10.86 | 15.27 | 19.47 | 13.13 | 10.78 | 5.47 | 14.47 | 13.44 |
| **70** | 7.95 | 17.78 | 22.25 | 13.13 | 16.63 | 20.49 | 14.66 | 26.55 | 22.46 | 23.44 | 20.02 | 14.79 | 16.05 | 19.52 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=1000 Hz

**Interrupted Conditioning then Blast Group (n=14)**

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **dB** | **2642** | **2644** | **2654** | **2655** | **2656** | **2657** | **2659** | **2660** | **2662** | **2664** | **2665** | **2683** | **2684** | **2685** |
| **20** | -9.49 | -9.87 | -9.74 | -9.25 | -9.72 | -9.24 | -9.59 | -8.79 | -9.08 | -9.76 | -10.12 | -10.53 | -9.61 | -9.75 |
| **25** | -10.66 | -9.03 | -10.13 | -9.72 | -9.53 | -8.61 | -9.81 | -8.96 | -10.42 | -10.30 | -8.84 | -10.82 | -9.38 | -9.54 |
| **30** | -9.60 | -9.30 | -8.97 | -10.07 | -9.65 | -9.39 | -10.05 | -9.49 | -8.66 | -9.76 | -9.34 | -9.65 | -9.80 | -10.42 |
| **35** | -9.45 | -9.13 | -8.70 | -9.42 | -9.49 | -8.81 | -8.45 | -9.30 | -9.60 | -9.85 | -8.74 | -10.29 | -9.70 | -7.99 |
| **40** | -9.84 | -8.46 | -9.37 | -9.80 | -10.11 | -8.06 | -9.81 | -9.15 | -10.54 | -9.56 | -8.18 | -10.82 | -9.88 | -8.40 |
| **45** | -8.90 | -9.33 | -9.48 | -9.55 | -9.93 | -8.12 | -9.85 | -9.34 | -8.92 | -9.51 | -7.60 | -10.73 | -8.20 | -7.59 |
| **50** | -9.33 | -8.22 | -8.91 | -6.82 | -6.67 | -0.42 | -7.68 | -9.25 | -8.06 | -7.93 | -2.93 | -4.83 | -2.93 | -0.92 |
| **55** | -2.39 | -7.96 | -6.60 | -1.70 | -1.23 | 5.56 | -2.96 | -9.27 | -1.92 | -2.73 | 4.19 | 3.52 | 2.50 | 3.11 |
| **60** | 5.94 | -1.13 | 1.37 | 3.14 | 7.12 | 11.09 | 2.54 | -7.51 | 3.92 | 0.60 | 10.39 | 11.77 | 6.41 | 10.28 |
| **65** | 13.44 | 0.30 | 10.21 | 11.96 | 11.97 | 14.85 | 4.84 | -1.86 | 14.66 | 2.21 | 10.46 | 18.47 | 16.20 | 15.27 |
| **70** | 21.76 | 6.60 | 18.41 | 17.18 | 14.44 | 18.14 | 7.14 | 6.25 | 25.37 | 11.12 | 20.45 | 24.51 | 18.66 | 16.02 |

**Continuous Conditioning then Blast Group (n=14)**

| **dB** | **2594** | **2595** | **2596** | **2597** | **2598** | **2599** | **2606** | **2607** | **2608** | **2609** | **2610** | **2611** | **2612** | **2613** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **20** | -9.54 | -8.10 | -9.23 | -9.34 | -8.49 | -10.24 | -10.92 | -7.83 | -10.66 | -8.87 | -10.03 | -8.48 | -9.37 | -10.31 |
| **25** | -9.65 | -7.58 | -11.17 | -8.84 | -7.01 | -10.24 | -9.91 | -7.83 | -9.86 | -9.53 | -9.98 | -9.09 | -10.35 | -10.14 |
| **30** | -10.34 | -8.48 | -9.01 | -9.42 | -8.13 | -9.76 | -10.37 | -8.52 | -9.93 | -9.67 | -7.88 | -9.51 | -9.15 | -9.93 |
| **35** | -9.46 | -10.09 | -8.57 | -9.82 | -8.24 | -9.53 | -10.47 | -7.76 | -9.60 | -9.59 | -8.71 | -8.90 | -10.05 | -8.96 |
| **40** | -9.62 | -7.60 | -9.82 | -10.18 | -8.48 | -11.57 | -10.00 | -8.55 | -10.04 | -11.53 | -8.55 | -9.13 | -9.28 | -9.35 |
| **45** | -9.42 | -6.80 | -9.10 | -7.61 | -8.84 | -9.92 | -9.48 | -6.62 | -10.56 | -10.12 | -8.04 | -8.20 | -9.12 | -5.91 |
| **50** | -9.66 | -3.33 | -6.52 | -5.16 | -5.65 | -8.45 | -3.80 | -0.16 | -7.99 | -6.22 | -8.74 | -5.81 | -9.24 | 1.03 |
| **55** | -8.04 | 2.04 | 2.50 | -0.68 | 1.34 | 0.66 | 3.29 | 3.88 | -5.08 | 0.04 | -4.02 | -2.58 | -3.13 | 7.63 |
| **60** | -2.04 | 5.33 | 7.42 | 7.77 | 8.80 | 9.63 | 9.80 | 4.13 | 3.56 | 7.67 | 3.25 | 4.62 | 2.59 | 12.60 |
| **65** | 1.88 | 11.71 | 10.16 | 17.39 | 12.00 | 16.32 | 14.99 | 11.44 | 8.03 | 11.83 | 9.41 | 9.40 | 9.95 | 15.43 |
| **70** | 14.28 | 23.63 | 13.97 | 23.64 | 14.81 | 21.25 | 16.76 | 22.50 | 13.24 | 14.43 | 10.72 | 8.72 | 17.84 | 19.87 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=1414 Hz

**Aged Normal Group (n=14)**

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
| 20 | -13.23 | -12.71 | -10.56 | -12.32 | -11.60 | -11.97 | -12.10 | -10.81 | -10.72 | -12.53 | -11.72 | -12.70 | -12.87 | -12.21 |
| 25 | -12.26 | -11.46 | -10.87 | -13.46 | -11.55 | -12.44 | -13.73 | -10.81 | -12.21 | -11.92 | -11.00 | -12.02 | -12.64 | -11.51 |
| 30 | -12.71 | -12.45 | -10.62 | -12.84 | -11.43 | -12.59 | -11.14 | -9.99 | -10.49 | -12.47 | -10.42 | -13.75 | -11.23 | -10.85 |
| 35 | -11.64 | -11.24 | -10.53 | -12.16 | -9.30 | -9.77 | -9.28 | -10.65 | -8.68 | -11.51 | -10.70 | -10.12 | -9.74 | -11.43 |
| 40 | -4.17 | -5.31 | -8.87 | -5.04 | -2.45 | -5.03 | -3.93 | -9.45 | -1.36 | -5.94 | -5.02 | -6.74 | -3.59 | -8.74 |
| 45 | 0.46 | 0.46 | -6.41 | 1.38 | 3.73 | -0.29 | 3.63 | -4.19 | 1.69 | 0.25 | 2.09 | -0.79 | 2.92 | -5.40 |
| 50 | -1.43 | 4.52 | -3.25 | 6.47 | 6.74 | 0.71 | 7.98 | 1.61 | 4.96 | 5.45 | 5.20 | 4.47 | 6.59 | -1.58 |
| 55 | -4.03 | 6.68 | -0.99 | 8.78 | 6.59 | -0.42 | 9.72 | 4.37 | 7.24 | 6.41 | 9.46 | 9.10 | 9.22 | 2.93 |
| 60 | 8.22 | 8.64 | 7.13 | 12.43 | 12.51 | 13.02 | 10.41 | 11.11 | 16.07 | 5.02 | 15.31 | 14.53 | 13.06 | 11.41 |
| 65 | 21.17 | 20.94 | 20.02 | 22.98 | 25.22 | 23.24 | 23.14 | 24.91 | 26.85 | 22.69 | 25.00 | 21.54 | 20.41 | 20.70 |
| 70 | 30.95 | 31.19 | 27.05 | 31.64 | 29.73 | 28.42 | 30.95 | 32.82 | 29.78 | 28.68 | 31.67 | 26.07 | 29.57 | 25.02 |

**Interrupted Conditioning Group (n=14)**

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -11.32 | -11.12 | -11.71 | -10.79 | -10.13 | -12.21 | -11.34 | -11.06 | -12.18 | -12.82 | -13.48 | -11.54 | -13.17 | -12.09 |
| 25 | -10.68 | -11.68 | -11.61 | -10.92 | -10.65 | -12.06 | -10.53 | -10.21 | -10.93 | -12.64 | -12.06 | -11.60 | -13.25 | -12.84 |
| 30 | -9.11 | -10.54 | -11.06 | -10.41 | -9.68 | -11.85 | -10.08 | -10.96 | -12.76 | -12.27 | -12.38 | -12.11 | -11.89 | -12.22 |
| 35 | -8.46 | -11.01 | -11.35 | -10.96 | -10.53 | -12.51 | -11.39 | -10.34 | -12.32 | -12.75 | -12.39 | -9.99 | -12.87 | -13.84 |
| 40 | -8.99 | -10.91 | -9.60 | -10.92 | -7.64 | -11.25 | -10.96 | -12.84 | -10.92 | -10.74 | -12.03 | -5.05 | -12.06 | -11.84 |
| 45 | -7.88 | -11.00 | -5.59 | -9.15 | -2.68 | -12.86 | -10.61 | -7.76 | -11.75 | -2.93 | -11.52 | 3.07 | -10.34 | -8.06 |
| 50 | -1.92 | -9.68 | 1.22 | -10.00 | 6.41 | -7.63 | -9.15 | 1.32 | -12.08 | 3.23 | -6.63 | 9.33 | -0.09 | 1.67 |
| 55 | 7.58 | -9.79 | 8.31 | -10.13 | 12.99 | -2.75 | -1.61 | 7.41 | -8.31 | 8.99 | 1.40 | 14.42 | 7.97 | 9.19 |
| 60 | 13.46 | -2.34 | 13.02 | -4.41 | 17.83 | 1.72 | 5.69 | 13.47 | 1.63 | 13.53 | 8.55 | 18.89 | 12.89 | 15.35 |
| 65 | 15.11 | 11.50 | 15.21 | 8.68 | 21.03 | 10.68 | 11.63 | 17.50 | 10.14 | 15.38 | 17.65 | 21.42 | 19.02 | 19.08 |
| 70 | 23.99 | 22.53 | 26.22 | 22.30 | 25.32 | 25.01 | 24.97 | 16.24 | 24.22 | 15.83 | 28.50 | 12.97 | 29.00 | 17.58 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=1414 Hz

Continuous Conditioning Group (n=14)

Animal #

| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -12.05 | -12.48 | -10.96 | -12.89 | -11.59 | -11.77 | -12.37 | -12.75 | -12.61 | -11.65 | -11.59 | -12.65 | -12.21 | -12.60 |
| 25 | -12.44 | -12.24 | -12.53 | -12.78 | -11.87 | -12.42 | -11.85 | -12.28 | -11.81 | -12.71 | -11.89 | -12.25 | -11.24 | -11.59 |
| 30 | -11.23 | -10.81 | -11.23 | -13.17 | -11.54 | -10.76 | -12.06 | -12.01 | -12.18 | -12.81 | -11.54 | -13.00 | -12.05 | -12.28 |
| 35 | -11.79 | -10.87 | -10.26 | -11.72 | -11.04 | -12.33 | -12.55 | -11.95 | -9.89 | -11.52 | -11.86 | -12.52 | -9.85 | -11.48 |
| 40 | -11.37 | -11.40 | -9.76 | -13.50 | -12.54 | -11.80 | -12.78 | -11.69 | -10.02 | -12.68 | -12.44 | -12.53 | -9.81 | -11.01 |
| 45 | -12.34 | -11.77 | -11.68 | -12.04 | -11.57 | -10.56 | -11.01 | -12.09 | -10.82 | -11.87 | -12.47 | -11.98 | -9.74 | -9.82 |
| 50 | -11.95 | -11.06 | -9.53 | -11.78 | -11.75 | -11.46 | -0.91 | -7.00 | -4.75 | -12.03 | -8.14 | -11.85 | -8.75 | -4.42 |
| 55 | -8.48 | -8.74 | -2.82 | -4.20 | -10.06 | -8.31 | 8.74 | 3.29 | 5.00 | -3.45 | -1.56 | -4.97 | -3.40 | 5.40 |
| 60 | -1.67 | -0.03 | 7.60 | 4.78 | -8.92 | 0.25 | 16.38 | 12.91 | 12.77 | 7.00 | 7.05 | 3.25 | 6.55 | 13.60 |
| 65 | 3.25 | 6.01 | 15.20 | 8.38 | 2.47 | 6.73 | 21.47 | 19.98 | 18.32 | 14.19 | 12.56 | 10.48 | 15.13 | 19.62 |
| 70 | 15.34 | 13.65 | 13.36 | 16.10 | 20.12 | 10.27 | 20.39 | 19.01 | 15.89 | 11.13 | 18.78 | 12.11 | 17.48 | 17.15 |

Blast Only Group (n=14)

| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -10.81 | -11.34 | -12.82 | -12.09 | -12.52 | -13.46 | -11.20 | -11.37 | -11.34 | -11.83 | -11.42 | -12.40 | -11.96 | -12.79 |
| 25 | -10.77 | -10.99 | -13.75 | -11.68 | -11.93 | -11.55 | -10.26 | -11.23 | -11.46 | -12.00 | -11.69 | -12.28 | -12.25 | -12.32 |
| 30 | -9.15 | -11.81 | -12.61 | -11.18 | -11.62 | -11.53 | -11.89 | -11.67 | -12.36 | -10.28 | -11.22 | -12.65 | -12.15 | -12.42 |
| 35 | -9.23 | -11.26 | -11.69 | -11.87 | -11.51 | -10.70 | -9.81 | -13.35 | -11.43 | -12.09 | -11.84 | -12.48 | -10.90 | -11.90 |
| 40 | -9.30 | -11.71 | -12.12 | -11.80 | -12.48 | -12.64 | -9.52 | -11.78 | -10.50 | -9.80 | -12.51 | -11.96 | -11.14 | -12.17 |
| 45 | -9.10 | -9.68 | -11.59 | -9.90 | -11.80 | -7.73 | -9.82 | -10.02 | -5.12 | -11.28 | -11.14 | -11.89 | -10.90 | -12.17 |
| 50 | -9.45 | -5.40 | -11.65 | -5.46 | -12.37 | -2.22 | -9.27 | -4.76 | -4.94 | -5.76 | -7.15 | -9.65 | -9.74 | -10.76 |
| 55 | -0.37 | 0.21 | -6.01 | 0.54 | -7.48 | 4.44 | -4.31 | -0.24 | -2.23 | 2.59 | 2.55 | -0.79 | -2.13 | -7.58 |
| 60 | 6.50 | 3.86 | 1.36 | 6.28 | -0.93 | 9.68 | 4.65 | 4.50 | -0.11 | 8.79 | 9.25 | 7.13 | 3.67 | -1.34 |
| 65 | 11.91 | 8.40 | 8.14 | 13.71 | 5.59 | 13.10 | 12.27 | 4.71 | 8.55 | 13.75 | 14.47 | 13.39 | 8.33 | 5.69 |
| 70 | 15.40 | 1.46 | 12.50 | 20.04 | 12.99 | 21.95 | 18.11 | 25.86 | 18.75 | 20.07 | 19.74 | 19.02 | 16.04 | 13.80 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=1414 Hz

Interrupted Conditioning then Blast Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2642 | 2644 | 2654 | 2655 | 2656 | 2657 | 2659 | 2660 | 2662 | 2664 | 2665 | 2683 | 2684 | 2685 |
| 20 | -12.19 | -11.93 | -12.68 | -12.89 | -12.43 | -12.11 | -12.21 | -12.62 | -12.46 | -12.32 | -11.40 | -12.72 | -11.89 | -11.96 |
| 25 | -11.56 | -11.53 | -12.57 | -11.77 | -12.73 | -11.82 | -11.48 | -12.15 | -12.65 | -11.93 | -11.10 | -13.50 | -11.84 | -11.75 |
| 30 | -11.89 | -11.34 | -12.09 | -12.15 | -11.71 | -11.09 | -11.61 | -12.48 | -11.78 | -11.71 | -11.37 | -12.36 | -11.18 | -11.84 |
| 35 | -11.20 | -11.24 | -12.53 | -12.06 | -11.85 | -12.46 | -11.30 | -11.67 | -11.83 | -12.26 | -10.85 | -11.73 | -11.52 | -10.74 |
| 40 | -10.95 | -11.22 | -11.67 | -11.90 | -12.41 | -12.09 | -11.90 | -12.17 | -12.47 | -12.03 | -11.27 | -12.62 | -11.50 | -10.46 |
| 45 | -10.65 | -11.31 | -11.45 | -10.80 | -10.18 | -9.28 | -11.46 | -12.28 | -12.05 | -11.50 | -11.49 | -11.06 | -10.15 | -10.86 |
| 50 | -8.84 | -10.92 | -12.53 | -11.74 | -7.74 | -9.31 | -12.57 | -12.85 | -10.12 | -12.09 | -9.74 | -9.30 | -10.27 | -4.88 |
| 55 | -0.60 | -9.60 | -11.51 | -7.63 | -0.71 | -5.62 | -11.86 | -12.39 | -4.45 | -6.20 | -6.24 | -1.67 | -5.88 | 1.14 |
| 60 | 6.41 | 0.69 | -8.65 | -6.74 | 6.15 | -0.55 | -8.75 | -11.23 | -0.45 | 0.25 | -0.09 | 4.16 | 2.10 | 7.25 |
| 65 | 11.02 | 8.18 | -0.43 | -2.30 | 11.77 | 4.65 | 1.88 | -7.04 | 5.04 | 9.63 | 5.31 | 7.06 | 10.27 | 9.91 |
| 70 | 13.56 | 16.58 | 5.11 | 8.46 | 15.42 | 13.37 | 8.62 | 5.11 | 9.15 | 15.52 | 17.19 | 3.07 | 18.13 | 11.52 |

Continuous Conditioning then Blast Group (n=14)

| dB | 2594 | 2595 | 2596 | 2597 | 2598 | 2599 | 2606 | 2607 | 2608 | 2609 | 2610 | 2611 | 2612 | 2613 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -10.39 | -10.62 | -11.60 | -13.25 | -10.40 | -11.93 | -12.72 | -11.65 | -12.45 | -11.76 | -11.61 | -10.54 | -12.33 | -11.57 |
| 25 | -10.31 | -11.24 | -11.65 | -11.12 | -10.05 | -11.07 | -14.86 | -11.90 | -11.65 | -12.21 | -12.04 | -9.93 | -11.10 | -11.49 |
| 30 | -9.90 | -10.69 | -12.24 | -11.75 | -10.96 | -11.49 | -12.63 | -11.10 | -11.93 | -11.61 | -10.73 | -10.78 | -11.15 | -12.43 |
| 35 | -10.07 | -9.31 | -10.30 | -11.04 | -9.93 | -12.87 | -11.02 | -10.24 | -10.96 | -11.83 | -12.17 | -11.06 | -11.28 | -10.74 |
| 40 | -9.53 | -11.00 | -11.59 | -9.49 | -10.05 | -12.82 | -11.21 | -9.58 | -10.01 | -10.65 | -10.16 | -9.76 | -10.96 | -11.15 |
| 45 | -10.43 | -8.35 | -10.90 | -9.99 | -11.15 | -10.37 | -11.08 | -10.28 | -10.09 | -12.42 | -9.74 | -9.82 | -12.07 | -11.31 |
| 50 | -9.30 | -1.93 | -9.20 | -6.90 | -10.01 | -11.56 | -2.52 | -5.51 | -10.08 | -7.83 | -9.64 | -9.51 | -10.70 | -5.52 |
| 55 | -7.90 | 4.49 | -5.23 | 0.86 | -7.74 | -9.74 | 2.28 | -2.24 | -8.51 | -3.78 | -4.49 | -3.51 | -6.93 | 2.73 |
| 60 | 1.52 | 10.15 | 1,68 | 7.11 | -3.61 | -8.98 | 5.57 | -7.70 | -3.31 | 3.06 | 0.92 | 2.19 | 1.32 | 9.24 |
| 65 | 10.19 | 15.76 | 12.77 | 9.21 | 5.61 | -6.98 | 8.73 | 7.04 | 3.04 | 8.31 | 5.30 | 7.86 | 5.98 | 13.61 |
| 70 | 16.47 | 22.67 | 20.69 | 7.34 | 10.93 | -0.94 | 14.62 | 22.50 | 11.05 | 12.54 | 10.77 | 13.89 | 11.24 | 18.46 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=2000 Hz

**Aged Normal Group (n=14)**

Animal #

| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -15.72 | -14.76 | -14.71 | -14.85 | -13.11 | -15.27 | -13.62 | -14.22 | -12.64 | -13.35 | -13.73 | -13.86 | -14.12 | -14.61 |
| 25 | -14.09 | -14.32 | -14.51 | -15.28 | -14.98 | -15.05 | -13.89 | -14.62 | -13.32 | -13.90 | -14.27 | -14.04 | -14.53 | -14.22 |
| 30 | -14.58 | -14.32 | -14.37 | -13.84 | -13.31 | -14.22 | -13.14 | -13.81 | -11.71 | -14.17 | -13.61 | -13.24 | -14.15 | -15.06 |
| 35 | -13.40 | -15.02 | -11.21 | -14.80 | -11.53 | -9.52 | -11.69 | -14.42 | -12.28 | -13.35 | -13.05 | -10.97 | -11.10 | -12.85 |
| 40 | -7.38 | -9.23 | -5.06 | -10.78 | -6.37 | -4.96 | -8.39 | -10.31 | -7.99 | -7.03 | -9.77 | -1.67 | -6.65 | -7.85 |
| 45 | 0.11 | -3.06 | 2.04 | -3.46 | -3.01 | 1.32 | -2.71 | -3.72 | -1.66 | 0.92 | -3.87 | 1.27 | 0.28 | -1.98 |
| 50 | 4.92 | 1.03 | 4.49 | 2.26 | 0.46 | 3.51 | 0.92 | 2.49 | 3.47 | 7.29 | 3.08 | 4.86 | 5.68 | 2.23 |
| 55 | 8.02 | 5.02 | 8.72 | 6.40 | 5.27 | 5.44 | 4.29 | 6.70 | 6.27 | 10.80 | 6.11 | 9.16 | 10.44 | 8.51 |
| 60 | 10.85 | 8.75 | 14.34 | 7.04 | 13.60 | 11.66 | 9.33 | 10.34 | 9.11 | 13.16 | 11.02 | 14.49 | 16.15 | 13.16 |
| 65 | 15.66 | 15.24 | 21.50 | 9.25 | 22.83 | 19.56 | 17.32 | 19.15 | 17.57 | 19.86 | 17.32 | 20.17 | 21.84 | 19.27 |
| 70 | 24.69 | 25.35 | 28.47 | 25.05 | 30.34 | 29.18 | 26.98 | 29.47 | 27.58 | 28.41 | 25.89 | 28.89 | 29.21 | 23.82 |

**Interrupted Conditioning Group (n=14)**

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -13.78 | -14.27 | -13.52 | -12.21 | -12.03 | -13.71 | -14.00 | -13.32 | -14.56 | -13.64 | -14.45 | -13.81 | -13.72 | -13.93 |
| 25 | -13.09 | -14.17 | -14.58 | -13.03 | -13.00 | -14.80 | -13.41 | -12.50 | -14.61 | -14.99 | -15.18 | -13.82 | -14.34 | -13.56 |
| 30 | -12.45 | -14.87 | -13.67 | -12.68 | -12.70 | -14.97 | -13.45 | -13.73 | -14.09 | -14.36 | -14.31 | -14.89 | -14.65 | -14.57 |
| 35 | -12.20 | -13.22 | -13.81 | -12.05 | -11.88 | -14.86 | -13.84 | -13.40 | -14.87 | -14.34 | -15.58 | -13.36 | -14.02 | -14.84 |
| 40 | -12.11 | -13.74 | -14.11 | -13.46 | -12.98 | -14.53 | -13.93 | -12.50 | -14.88 | -16.67 | -14.05 | -13.75 | -13.63 | -14.47 |
| 45 | -10.24 | -14.05 | -13.67 | -12.18 | -13.06 | -14.14 | -12.27 | -13.68 | -14.33 | -12.37 | -13.93 | -11.40 | -6.31 | -13.75 |
| 50 | -10.90 | -14.09 | -12.84 | -12.00 | -10.00 | -12.87 | -10.25 | -11.52 | -14.34 | -8.81 | -10.42 | -4.84 | 2.25 | -12.83 |
| 55 | -1.75 | -12.35 | -7.34 | -5.62 | -4.27 | -6.94 | -8.12 | -4.87 | -11.79 | 0.29 | -0.90 | 2.18 | 9.29 | -3.78 |
| 60 | 5.58 | -7.17 | -1.61 | 4.04 | 5.13 | 1.89 | -2.84 | 4.52 | -5.96 | 5.83 | 7.20 | 9.02 | 15.10 | 5.41 |
| 65 | 13.44 | -3.95 | 8.05 | 10.36 | 13.32 | 10.75 | 7.77 | 11.70 | -0.05 | 11.14 | 14.17 | 15.23 | 20.94 | 13.30 |
| 70 | 21.88 | 8.15 | 17.40 | 16.74 | 21.97 | 18.58 | 16.46 | 22.10 | 10.71 | 18.69 | 20.69 | 21.42 | 25.36 | 19.48 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=2000 Hz

Continuous Conditioning Group (n=14)

Animal #

| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -14.65 | -13.43 | -15.42 | -14.31 | -13.56 | -13.87 | -14.21 | -14.35 | -14.78 | -14.57 | -14.21 | -14.81 | -13.86 | -14.76 |
| 25 | -15.38 | -13.85 | -13.14 | -14.92 | -14.41 | -14.27 | -12.93 | -13.28 | -13.68 | -13.81 | -14.48 | -15.31 | -13.43 | -14.68 |
| 30 | -14.96 | -14.06 | -15.67 | -14.37 | -13.61 | -14.88 | -14.77 | -15.10 | -14.43 | -15.01 | -14.37 | -15.53 | -13.16 | -13.29 |
| 35 | -14.89 | -13.04 | -14.48 | -14.89 | -14.90 | -14.18 | -14.27 | -14.08 | -13.75 | -15.12 | -13.70 | -13.43 | -14.41 | -13.74 |
| 40 | -14.55 | -14.29 | -13.84 | -15.09 | -13.99 | -13.93 | -14.59 | -14.57 | -13.40 | -14.77 | -14.67 | -13.27 | -13.39 | -14.32 |
| 45 | -15.08 | -13.31 | -13.21 | -14.64 | -14.37 | -14.08 | -13.15 | -14.91 | -13.32 | -14.09 | -12.76 | -14.92 | -11.98 | -14.61 |
| 50 | -15.08 | -12.18 | -14.28 | -14.37 | -14.23 | -11.88 | -15.33 | -11.98 | -13.56 | -14.11 | -14.22 | -14.93 | -12.29 | -13.90 |
| 55 | -15.03 | -10.92 | -10.48 | -14.14 | -13.43 | -13.12 | -9.81 | -4.84 | -9.82 | -9.86 | -11.74 | -12.56 | -9.40 | -8.46 |
| 60 | -10.26 | -1.65 | -1.79 | -8.77 | -9.10 | -2.62 | 2.25 | 5.83 | 1.57 | -0.27 | -1.33 | -3.67 | -2.43 | 0.67 |
| 65 | -5.34 | 8.17 | 9.19 | 0.24 | 3.36 | 7.61 | 13.41 | 14.93 | 11.61 | 8.82 | 10.50 | 6.97 | 9.15 | 10.31 |
| 70 | 9.34 | 17.47 | 17.60 | 12.71 | 14.90 | 16.32 | 21.78 | 21.60 | 20.36 | 16.97 | 19.90 | 15.02 | 18.82 | 16.83 |

Blast Only Group (n=14)

| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -12.89 | -13.03 | -14.22 | -13.68 | -14.36 | -13.86 | -12.57 | -13.85 | -14.26 | -14.08 | -14.75 | -14.53 | -14.20 | -14.77 |
| 25 | -12.17 | -13.06 | -13.75 | -14.74 | -14.62 | -13.66 | -11.49 | -12.86 | -13.31 | -14.05 | -14.14 | -14.12 | -13.61 | -14.05 |
| 30 | -15.40 | -13.62 | -13.72 | -15.03 | -14.43 | -14.24 | -12.79 | -14.43 | -15.25 | -14.28 | -14.44 | -14.36 | -13.77 | -14.25 |
| 35 | -13.31 | -12.78 | -13.95 | -15.15 | -14.52 | -14.90 | -12.47 | -14.70 | -11.80 | -14.34 | -13.06 | -13.59 | -12.95 | -13.62 |
| 40 | -11.67 | -13.41 | -13.97 | -13.59 | -15.76 | -14.07 | -11.58 | -13.49 | -10.35 | -13.97 | -12.76 | -14.56 | -13.80 | -13.67 |
| 45 | -12.30 | -13.09 | -13.00 | -15.06 | -13.78 | -13.62 | -13.86 | -10.90 | -10.55 | -13.12 | -14.37 | -14.91 | -14.75 | -13.17 |
| 50 | -10.24 | -10.55 | -14.12 | -11.05 | -11.10 | -12.59 | -11.17 | -7.31 | -4.04 | -13.73 | -11.92 | -13.34 | -13.00 | -13.42 |
| 55 | -3.67 | -3.84 | -7.97 | -3.98 | -3.87 | -8.40 | -3.35 | -3.62 | 4.03 | -11.92 | -10.35 | -9.67 | -7.35 | -12.75 |
| 60 | 4.00 | 4.73 | 1.01 | 3.68 | 5.09 | -1.43 | 4.48 | -0.05 | 9.96 | -7.16 | -8.18 | -1.73 | 0.19 | -9.72 |
| 65 | 9.53 | 13.38 | 7.22 | 9.56 | 11.94 | 4.14 | 10.00 | 4.54 | 15.25 | -1.79 | -1.19 | 4.91 | 6.75 | -7.68 |
| 70 | 13.85 | 20.78 | 10.94 | 14.96 | 16.95 | 11.80 | 13.77 | 11.55 | 19.68 | 3.19 | 7.69 | 11.79 | 11.41 | -1.01 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=2000 Hz

Interrupted Conditioning then Blast Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2642 | 2644 | 2654 | 2655 | 2656 | 2657 | 2659 | 2660 | 2662 | 2664 | 2665 | 2683 | 2684 | 2685 |
| 20 | -14.52 | -15.00 | -14.78 | -14.49 | -14.87 | -13.22 | -14.38 | -14.33 | -13.94 | -14.43 | -14.54 | -14.26 | -14.55 | -14.24 |
| 25 | -13.68 | -13.98 | -14.97 | -14.60 | -14.00 | -13.68 | -14.34 | -14.61 | -14.06 | -14.62 | -14.24 | -15.01 | -14.87 | -14.20 |
| 30 | -14.18 | -14.15 | -14.42 | -14.31 | -14.86 | -14.26 | -13.60 | -14.50 | -14.90 | -14.31 | -14.81 | -14.42 | -15.27 | -13.76 |
| 35 | -13.78 | -13.97 | -14.16 | -14.58 | -14.32 | -15.86 | -13.71 | -14.31 | -14.84 | -13.44 | -15.13 | -13.00 | -13.75 | -13.81 |
| 40 | -14.43 | -14.76 | -14.30 | -14.90 | -14.78 | -13.05 | -14.00 | -13.69 | -14.00 | -14.89 | -14.31 | -14.83 | -14.15 | -13.48 |
| 45 | -13.95 | -14.72 | -13.72 | -14.02 | -14.40 | -12.32 | -14.52 | -13.93 | -13.88 | -14.18 | -13.15 | -14.33 | -14.63 | -12.40 |
| 50 | -12.87 | -15.32 | -13.53 | -14.17 | -13.37 | -5.79 | -13.12 | -13.99 | -11.60 | -14.85 | -14.28 | -14.25 | -14.15 | -12.43 |
| 55 | -7.07 | -12.86 | -13.82 | -9.34 | -7.40 | 1.68 | -10.06 | -13.99 | -8.11 | -13.49 | -13.31 | -11.89 | -10.05 | -10.02 |
| 60 | 1.31 | -7.11 | -12.66 | -3.65 | -3.82 | 8.25 | -1.32 | -13.37 | -0.87 | -6.65 | -7.03 | -7.15 | -3.17 | -6.50 |
| 65 | 8.47 | -0.61 | -9.45 | 3.20 | 3.02 | 13.80 | 5.14 | -12.89 | 7.46 | 0.55 | -4.34 | 1.40 | 6.03 | 1.99 |
| 70 | 12.46 | 5.68 | -4.44 | 7.60 | 11.30 | 13.67 | 4.03 | -3.22 | 13.63 | 6.18 | 1.85 | 9.81 | 12.14 | 10.15 |

Continuous Conditioning then Blast Group (n=14)

| dB | 2594 | 2595 | 2596 | 2597 | 2598 | 2599 | 2606 | 2607 | 2608 | 2609 | 2610 | 2611 | 2612 | 2613 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -14.30 | -11.65 | -14.84 | -14.68 | -12.91 | -14.25 | -14.07 | -14.09 | -13.67 | -15.07 | -13.87 | -13.81 | -13.78 | -14.40 |
| 25 | -14.70 | -12.39 | -14.64 | -13.34 | -13.63 | -15.29 | -14.25 | -12.21 | -13.32 | -13.53 | -13.26 | -13.38 | -13.82 | -13.21 |
| 30 | -14.43 | -11.78 | -15.21 | -12.85 | -13.00 | -14.27 | -14.09 | -12.31 | -13.34 | -12.65 | -13.62 | -13.63 | -13.96 | -13.64 |
| 35 | -14.72 | -12.53 | -14.55 | -12.87 | -12.47 | -13.48 | -14.06 | -13.02 | -13.50 | -13.81 | -13.21 | -14.92 | -14.10 | -12.77 |
| 40 | -14.35 | -11.47 | -13.61 | -14.07 | -13.37 | -13.09 | -14.44 | -11.50 | -14.93 | -12.70 | -12.84 | -12.48 | -14.21 | -13.28 |
| 45 | -13.30 | -11.62 | -13.32 | -11.56 | -13.48 | -15.03 | -14.89 | -12.06 | -12.70 | -12.47 | -12.56 | -12.80 | -13.56 | -13.53 |
| 50 | -8.62 | -7.30 | -11.75 | -11.91 | -13.54 | -12.93 | -9.53 | -8.80 | -11.77 | -13.14 | -13.93 | -12.03 | -13.18 | -12.71 |
| 55 | 0.53 | 1.80 | -4.26 | -14.32 | -10.43 | -13.17 | -3.77 | -4.37 | -14.67 | -12.86 | -13.33 | -7.57 | -13.43 | -8.57 |
| 60 | 7.27 | 9.94 | 2.82 | -10.93 | -8.46 | -10.81 | 2.94 | 3.20 | -8.05 | -7.35 | -8.40 | -1.55 | -10.86 | 0.69 |
| 65 | 10.99 | 16.36 | 8.89 | -11.57 | -4.67 | -8.23 | 8.96 | 8.69 | -1.10 | -0.26 | -3.76 | 5.05 | -7.04 | 10.79 |
| 70 | 12.22 | 20.78 | 11.83 | 6.72 | 2.93 | 0.84 | 14.30 | 13.10 | 2.13 | 9.08 | -4.63 | 9.12 | 1.48 | 19.12 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=2828 Hz

**Aged Normal Group (n=14)**

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
| 20 | -18.50 | -17.55 | -16.46 | -16.96 | -17.09 | -17.06 | -17.06 | -17.33 | -15.61 | -16.25 | -17.28 | -17.41 | -18.11 | -17.78 |
| 25 | -17.20 | -17.65 | -16.50 | -17.29 | -16.59 | -15.51 | -17.57 | -17.51 | -15.64 | -16.72 | -16.83 | -16.83 | -18.31 | -17.90 |
| 30 | -15.97 | -16.71 | -13.67 | -16.71 | -14.70 | -16.09 | -16.30 | -17.83 | -15.39 | -17.66 | -16.39 | -17.49 | -16.56 | -12.64 |
| 35 | -14.72 | -13.14 | -11.79 | -13.27 | -9.53 | -14.06 | -11.10 | -17.27 | -14.95 | -13.25 | -13.27 | -13.28 | -14.70 | -8.90 |
| 40 | -7.85 | -5.95 | -6.01 | -7.75 | -4.09 | -9.32 | -6.97 | -12.99 | -10.53 | -7.63 | -8.51 | -9.82 | -7.88 | -4.58 |
| 45 | -4.28 | -1.59 | -2.58 | -3.60 | 0.87 | -9.65 | -3.56 | -6.86 | -6.41 | -4.72 | -5.41 | -3.56 | -5.35 | 0.66 |
| 50 | 0.78 | 2.09 | 2.38 | 2.46 | 5.71 | -3.97 | 2.46 | -3.28 | 0.31 | 0.27 | -0.10 | 0.28 | 3.74 | 7.31 |
| 55 | 6.08 | 6.64 | 9.10 | 7.11 | 11.25 | 3.22 | 9.11 | 2.34 | 5.30 | 5.40 | 5.79 | 8.64 | 9.12 | 13.99 |
| 60 | 12.40 | 14.44 | 17.10 | 13.41 | 19.27 | 11.41 | 16.49 | 12.68 | 11.79 | 13.86 | 11.68 | 17.46 | 14.35 | 21.91 |
| 65 | 21.05 | 23.86 | 21.53 | 21.90 | 26.06 | 20.31 | 24.83 | 23.30 | 21.32 | 22.85 | 16.16 | 24.11 | 19.70 | 17.29 |
| 70 | 17.02 | 13.17 | 27.17 | 24.71 | 19.45 | 18.29 | 25.44 | 25.64 | 25.78 | 23.26 | 25.30 | 24.02 | 23.39 | 33.75 |

**Interrupted Conditioning Group (n=14)**

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -17.42 | -16.96 | -16.53 | -15.40 | -16.56 | -16.89 | -16.38 | -17.40 | -17.64 | -17.65 | -16.81 | -17.08 | -17.47 | -16.76 |
| 25 | -16.53 | -16.87 | -16.45 | -16.06 | -16.33 | -16.21 | -15.64 | -16.18 | -16.03 | -16.47 | -17.37 | -16.85 | -17.25 | -18.00 |
| 30 | -16.78 | -16.62 | -16.03 | -14.99 | -16.15 | -16.89 | -16.37 | -16.48 | -16.67 | -17.89 | -16.74 | -15.97 | -16.30 | -17.22 |
| 35 | -17.12 | -16.72 | -15.86 | -15.42 | -16.17 | -17.04 | -16.29 | -16.19 | -16.97 | -15.72 | -16.55 | -16.40 | -16.13 | -17.59 |
| 40 | -16.93 | -17.09 | -15.98 | -14.77 | -16.04 | -15.31 | -15.83 | -16.96 | -17.24 | -16.47 | -16.90 | -15.20 | -10.81 | -17.65 |
| 45 | -16.81 | -16.87 | -15.53 | -15.47 | -14.75 | -16.65 | -16.36 | -17.19 | -17.53 | -14.87 | -16.30 | -9.58 | -4.17 | -16.50 |
| 50 | -12.54 | -16.63 | -16.78 | -11.38 | -10.56 | -16.22 | -15.12 | -10.53 | -15.50 | -10.92 | -15.48 | -2.87 | 3.41 | -10.05 |
| 55 | -8.26 | -15.83 | -6.74 | -6.76 | -4.94 | -8.92 | -11.89 | -1.41 | -7.80 | -2.26 | -9.20 | 4.29 | 8.89 | -3.23 |
| 60 | 1.07 | -12.42 | -2.59 | 1.12 | 4.45 | -0.88 | -3.05 | 7.69 | -3.95 | 3.96 | 0.29 | 10.42 | 13.41 | 3.93 |
| 65 | 7.92 | -0.77 | 2.84 | 7.52 | 9.67 | 4.35 | 5.13 | 16.03 | 1.96 | 14.77 | 9.94 | 13.12 | 17.76 | 9.62 |
| 70 | 7.66 | 11.52 | 13.47 | 9.61 | 18.10 | 15.46 | 13.25 | 14.04 | 21.52 | 19.72 | 13.81 | 23.27 | 15.34 | 16.05 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=2828 Hz

Continuous Conditioning Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
| 20 | -17.22 | -17.18 | -16.88 | -17.53 | -17.08 | -17.47 | -16.46 | -18.01 | -16.57 | -17.84 | -17.06 | -17.31 | -17.08 | -15.80 |
| 25 | -17.16 | -16.20 | -16.90 | -17.37 | -17.40 | -18.06 | -16.70 | -17.84 | -17.38 | -17.22 | -17.28 | -17.44 | -17.40 | -17.06 |
| 30 | -16.68 | -16.77 | -17.12 | -16.22 | -16.22 | -17.18 | -16.94 | -17.18 | -16.96 | -16.63 | -16.31 | -17.34 | -15.75 | -15.22 |
| 35 | -16.36 | -17.20 | -17.49 | -17.78 | -18.00 | -17.37 | -17.15 | -16.81 | -16.40 | -17.31 | -16.09 | -16.84 | -16.94 | -17.51 |
| 40 | -17.80 | -16.30 | -17.84 | -17.62 | -17.88 | -16.99 | -16.78 | -17.36 | -18.18 | -17.56 | -15.75 | -17.19 | -16.84 | -15.55 |
| 45 | -17.29 | -16.54 | -17.19 | -17.74 | -16.24 | -16.52 | -15.84 | -16.75 | -18.81 | -17.44 | -15.52 | -16.43 | -14.36 | -16.08 |
| 50 | -16.23 | -15.46 | -15.63 | -16.89 | -16.42 | -14.46 | -16.56 | -15.59 | -13.06 | -16.24 | -15.32 | -17.35 | -7.85 | -11.93 |
| 55 | -9.76 | -11.87 | -13.46 | -12.65 | -12.31 | -6.36 | -14.50 | -1.07 | -10.28 | -11.17 | -6.82 | -12.03 | 0.90 | -7.09 |
| 60 | -2.69 | -0.86 | -1.43 | -4.06 | -4.18 | 3.12 | -7.56 | 11.80 | -3.22 | -0.88 | 2.69 | -6.57 | 10.59 | 1.14 |
| 65 | 5.72 | 8.01 | 12.56 | 7.14 | 6.02 | 9.67 | 1.50 | 21.88 | 8.43 | 10.02 | 12.86 | 0.46 | 21.03 | 10.29 |
| 70 | 13.18 | 21.55 | 25.58 | 17.76 | 13.89 | 16.29 | 13.42 | 25.94 | 21.60 | 21.38 | 23.13 | 7.58 | 30.05 | 18.76 |

Blast Only Group (n=14)

| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -17.25 | -16.11 | -17.96 | -16.33 | -16.54 | -17.05 | -15.95 | -16.71 | -16.28 | -15.90 | -17.99 | -16.59 | -17.61 | -16.78 |
| 25 | -16.49 | -16.55 | -17.50 | -17.99 | -17.57 | -17.50 | -16.03 | -17.47 | -16.17 | -15.37 | -16.79 | -17.93 | -16.86 | -17.34 |
| 30 | -16.97 | -15.55 | -18.49 | -15.74 | -17.44 | -17.39 | -15.31 | -17.21 | -18.13 | -15.60 | -17.85 | -16.75 | -16.72 | -17.40 |
| 35 | -14.78 | -17.10 | -18.21 | -18.31 | -16.15 | -16.82 | -16.03 | -16.12 | -15.61 | -16.71 | -16.91 | -16.37 | -15.93 | -16.36 |
| 40 | -17.03 | -15.83 | -18.56 | -17.70 | -17.58 | -15.78 | -16.36 | -16.12 | -16.16 | -15.74 | -18.36 | -17.65 | -17.58 | -16.55 |
| 45 | -15.97 | -16.33 | -16.05 | -15.33 | -15.75 | -15.91 | -14.98 | -17.15 | -13.70 | -16.54 | -17.50 | -17.83 | -16.75 | -14.19 |
| 50 | -15.64 | -9.51 | -16.21 | -15.31 | -11.74 | -16.40 | -16.83 | -13.04 | -6.05 | -16.38 | -15.10 | -17.23 | -15.72 | -8.29 |
| 55 | -12.71 | -1.18 | -13.71 | -8.17 | -2.65 | -13.39 | -14.84 | -3.80 | 0.37 | -15.67 | -6.63 | -16.52 | -12.02 | -1.68 |
| 60 | -11.53 | 6.48 | -5.12 | 0.48 | 3.20 | -8.29 | -11.89 | 3.28 | 6.08 | -14.59 | 1.34 | -11.10 | -2.75 | 3.88 |
| 65 | -6.38 | 10.25 | 0.14 | 6.87 | 7.03 | -10.79 | -7.99 | 4.66 | 9.81 | -7.67 | 3.90 | -3.11 | 3.71 | 4.78 |
| 70 | 4.22 | 13.95 | 7.06 | 10.41 | -5.45 | 4.81 | -2.94 | 9.58 | 7.75 | 0.72 | 4.75 | 4.32 | 10.33 | 11.80 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=2828 Hz

**Interrupted Conditioning then Blast Group (n=14)**

**Animal #**

| dB | 2642 | 2644 | 2654 | 2655 | 2656 | 2657 | 2659 | 2660 | 2662 | 2664 | 2665 | 2683 | 2684 | 2685 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **20** | -16.94 | -17.09 | -16.47 | -17.07 | -17.12 | -16.58 | -16.48 | -16.65 | -16.98 | -17.05 | -16.27 | -18.31 | -17.00 | -17.79 |
| **25** | -16.67 | -17.66 | -16.72 | -16.57 | -16.96 | -16.14 | -17.53 | -16.71 | -17.65 | -17.84 | -17.33 | -17.65 | -16.71 | -17.06 |
| **30** | -16.22 | -17.06 | -16.59 | -16.70 | -17.16 | -15.81 | -17.11 | -16.97 | -16.15 | -17.02 | -17.22 | -17.06 | -16.44 | -15.95 |
| **35** | -16.58 | -17.37 | -16.57 | -16.87 | -17.06 | -15.84 | -16.67 | -16.78 | -16.26 | -17.17 | -16.56 | -16.94 | -15.90 | -16.30 |
| **40** | -17.22 | -17.39 | -16.28 | -16.60 | -16.96 | -16.36 | -16.71 | -16.24 | -16.08 | -17.74 | -16.99 | -17.26 | -15.53 | -16.64 |
| **45** | -14.84 | -16.27 | -15.94 | -16.11 | -13.81 | -14.23 | -14.52 | -16.12 | -18.30 | -17.13 | -15.34 | -16.41 | -16.97 | -16.12 |
| **50** | -11.09 | -14.66 | -16.59 | -16.56 | -7.10 | -7.79 | -9.28 | -16.87 | -12.67 | -15.53 | -15.32 | -16.15 | -14.00 | -15.18 |
| **55** | -6.88 | -10.85 | -13.59 | -8.28 | 1.34 | -0.72 | -1.33 | -15.78 | -3.34 | -9.36 | -10.98 | -9.44 | -9.95 | -13.24 |
| **60** | -2.66 | -4.30 | -13.24 | -3.44 | 6.39 | 5.17 | 4.30 | -15.74 | 5.48 | -0.64 | -7.01 | -2.93 | -1.22 | -9.60 |
| **65** | -6.30 | 1.25 | -0.80 | 2.14 | 8.42 | 14.38 | 3.70 | -4.89 | 12.05 | 4.67 | 4.64 | 5.75 | 3.66 | 0.45 |
| **70** | 12.30 | 4.80 | 7.42 | 5.52 | 9.06 | 22.19 | 16.22 | 5.75 | 13.09 | 8.82 | 13.18 | 10.88 | 10.34 | 10.11 |

**Continuous Conditioning then Blast Group (n=14)**

| dB | 2594 | 2595 | 2596 | 2597 | 2598 | 2599 | 2606 | 2607 | 2608 | 2609 | 2610 | 2611 | 2612 | 2613 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **20** | -17.16 | -15.58 | -18.08 | -15.93 | -15.72 | -16.57 | -17.70 | -17.68 | -17.08 | -16.12 | -17.31 | -16.25 | -17.12 | -16.09 |
| **25** | -18.06 | -17.25 | -17.38 | -15.97 | -15.65 | -16.08 | -17.65 | -16.94 | -17.68 | -16.28 | -16.56 | -15.03 | -16.53 | -15.56 |
| **30** | -17.55 | -16.75 | -16.75 | -15.64 | -15.47 | -14.83 | -19.00 | -18.58 | -17.33 | -15.92 | -17.99 | -15.97 | -16.05 | -17.34 |
| **35** | -16.21 | -16.30 | -15.77 | -15.94 | -15.61 | -15.08 | -17.94 | -18.28 | -17.72 | -16.38 | -17.15 | -15.26 | -16.91 | -15.91 |
| **40** | -16.05 | -14.99 | -16.90 | -15.36 | -17.09 | -16.22 | -18.98 | -16.09 | -15.84 | -16.52 | -16.45 | -15.68 | -17.04 | -15.83 |
| **45** | -15.69 | -15.22 | -16.58 | -16.22 | -15.81 | -17.79 | -14.61 | -14.86 | -15.28 | -15.15 | -17.71 | -15.04 | -16.77 | -16.03 |
| **50** | -15.20 | -8.21 | -16.25 | -16.09 | -15.41 | -16.59 | -16.36 | -9.68 | -9.84 | -12.02 | -14.28 | -13.87 | -16.75 | -16.15 |
| **55** | -14.04 | -1.01 | -10.55 | -13.96 | -14.74 | -14.98 | -8.28 | -6.29 | -1.73 | -6.18 | -11.88 | -15.69 | -14.85 | -10.65 |
| **60** | -7.00 | 5.51 | -6.82 | -10.17 | -10.56 | -7.95 | -4.52 | -2.35 | 3.62 | 0.86 | -3.64 | -10.62 | -13.49 | 0.26 |
| **65** | 0.53 | 10.70 | 5.16 | 3.29 | 0.25 | 0.59 | -1.81 | -8.82 | 9.44 | 8.86 | 6.58 | -0.22 | -9.01 | 7.51 |
| **70** | 10.11 | 3.08 | 17.91 | 11.77 | 11.85 | 8.58 | 5.51 | 11.06 | 19.40 | 13.05 | 16.57 | 11.55 | 2.19 | 12.19 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=4000 Hz

Aged Normal Group (n=14)

Animal #

| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -18.95 | -19.66 | -18.87 | -18.88 | -18.20 | -19.78 | -19.68 | -20.46 | -18.55 | -19.90 | -19.62 | -19.09 | -20.44 | -20.16 |
| 25 | -18.26 | -20.05 | -17.40 | -19.91 | -18.03 | -14.89 | -19.53 | -19.26 | -18.18 | -18.53 | -20.17 | -15.81 | -17.34 | -15.72 |
| 30 | -14.56 | -15.28 | -12.31 | -15.47 | -13.94 | -9.35 | -13.49 | -17.19 | -16.62 | -19.83 | -15.25 | -12.18 | -12.48 | -9.32 |
| 35 | -7.74 | -7.46 | -6.16 | -8.87 | -8.30 | -3.56 | -8.76 | -9.51 | -10.76 | -11.89 | -8.20 | -5.63 | -6.62 | -3.62 |
| 40 | -1.04 | -0.98 | -1.20 | -3.93 | -3.54 | 0.58 | -2.08 | -3.82 | -4.81 | -5.88 | -3.97 | -0.89 | -1.11 | 1.21 |
| 45 | 3.90 | 3.91 | 3.39 | 1.12 | 1.76 | 4.65 | 2.79 | 1.46 | 0.19 | -0.07 | 1.22 | 3.64 | 3.56 | 6.16 |
| 50 | 8.69 | 7.79 | 8.74 | 5.69 | 8.25 | 10.02 | 7.81 | 6.65 | 5.35 | 6.39 | 7.28 | 8.79 | 8.72 | 11.65 |
| 55 | 13.61 | 10.47 | 15.58 | 10.44 | 15.45 | 17.10 | 13.17 | 12.38 | 10.78 | 11.44 | 11.52 | 14.68 | 14.55 | 19.02 |
| 60 | 20.64 | 18.12 | 22.72 | 17.65 | 22.92 | 24.89 | 20.44 | 20.08 | 19.17 | 19.20 | 17.91 | 23.06 | 21.10 | 22.56 |
| 65 | 25.14 | 22.32 | 23.68 | 22.79 | 25.17 | 27.28 | 25.96 | 24.69 | 25.22 | 24.21 | 24.80 | 23.02 | 21.19 | 10.90 |
| 70 | 18.07 | 14.85 | 31.06 | 17.89 | 20.89 | 25.13 | 20.23 | 14.03 | 23.11 | 22.47 | 18.62 | 26.70 | 26.39 | 32.11 |

Interrupted Conditioning Group (n=14)

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -19.82 | -19.72 | -19.21 | -17.86 | -19.63 | -19.97 | -20.00 | -20.24 | -19.70 | -19.48 | -20.00 | -19.09 | -20.93 | -20.09 |
| 25 | -19.58 | -19.61 | -18.50 | -17.00 | -19.88 | -19.23 | -19.42 | -19.21 | -19.44 | -19.55 | -19.00 | -18.97 | -18.60 | -20.48 |
| 30 | -20.24 | -20.03 | -18.91 | -17.08 | -18.50 | -20.11 | -19.81 | -19.93 | -19.44 | -20.97 | -20.16 | -19.93 | -19.80 | -19.41 |
| 35 | -18.34 | -20.18 | -20.05 | -18.29 | -17.63 | -19.92 | -20.27 | -19.24 | -19.75 | -18.82 | -19.44 | -17.63 | -17.47 | -18.34 |
| 40 | -20.27 | -19.07 | -17.86 | -17.40 | -12.53 | -17.10 | -18.77 | -18.02 | -17.81 | -18.12 | -19.28 | -12.83 | -14.97 | -17.56 |
| 45 | -18.07 | -18.37 | -16.57 | -10.91 | -6.16 | -12.09 | -19.74 | -14.84 | -16.09 | -18.97 | -10.35 | -6.52 | -9.87 | -16.19 |
| 50 | -8.76 | -15.26 | -7.97 | -4.98 | 0.32 | -7.07 | -8.64 | -7.50 | -5.10 | -5.23 | -1.94 | 0.69 | -3.65 | -11.68 |
| 55 | 1.88 | -5.93 | -0.25 | 5.95 | 9.19 | 1.81 | 0.25 | 3.08 | 4.07 | 8.31 | 5.05 | 8.70 | 4.33 | 0.60 |
| 60 | 11.60 | 4.11 | 8.01 | 12.88 | 18.99 | 8.05 | 12.67 | 13.56 | 12.24 | 18.73 | 12.78 | 16.17 | 13.41 | 13.89 |
| 65 | 19.28 | 13.45 | 18.52 | 18.32 | 23.54 | 20.62 | 20.44 | 20.94 | 14.10 | 19.68 | 17.07 | 16.28 | 15.99 | 21.14 |
| 70 | 20.89 | 23.81 | 23.68 | 13.40 | 18.43 | 20.69 | 23.70 | 21.32 | 28.81 | 25.41 | 20.02 | 25.14 | 22.83 | 14.88 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=4000 Hz

Continuous Conditioning Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
| 20 | -19.21 | -19.69 | -20.25 | -20.30 | -19.99 | -19.66 | -20.14 | -20.66 | -19.27 | -19.89 | -19.77 | -20.30 | -18.99 | -19.55 |
| 25 | -19.91 | -20.22 | -20.63 | -20.53 | -19.66 | -19.56 | -19.88 | -19.34 | -19.96 | -19.62 | -19.00 | -20.87 | -19.16 | -20.23 |
| 30 | -19.87 | -20.62 | -19.42 | -19.34 | -21.07 | -19.93 | -20.62 | -20.96 | -19.46 | -18.57 | -20.63 | -20.56 | -19.41 | -19.17 |
| 35 | -20.77 | -20.28 | -20.39 | -19.66 | -19.90 | -19.06 | -20.22 | -14.29 | -18.90 | -19.35 | -18.15 | -19.56 | -18.43 | -18.84 |
| 40 | -17.37 | -19.75 | -18.69 | -19.09 | -20.53 | -17.96 | -20.51 | -7.47 | -16.57 | -14.22 | -14.70 | -15.59 | -13.82 | -18.03 |
| 45 | -13.00 | -13.83 | -18.68 | -16.93 | -18.72 | -10.96 | -17.83 | -1.71 | -9.80 | -9.64 | -8.05 | -10.46 | -11.99 | -13.75 |
| 50 | -3.16 | -3.83 | -14.78 | -8.49 | -12.30 | -0.50 | -17.69 | 1.07 | -5.30 | -6.37 | -5.18 | -7.68 | -5.01 | -7.41 |
| 55 | 6.05 | 4.90 | 2.34 | 2.30 | -2.32 | 8.30 | -8.68 | 4.48 | 2.02 | -6.16 | 0.99 | -2.78 | 9.20 | -0.01 |
| 60 | 13.88 | 13.05 | 15.21 | 10.46 | 8.11 | 15.21 | 7.14 | 19.40 | 15.55 | 10.43 | 13.82 | 10.96 | 18.83 | 10.02 |
| 65 | 14.72 | 19.56 | 15.93 | 14.24 | 18.37 | 15.77 | 20.86 | 21.98 | 24.03 | 21.39 | 22.85 | 19.31 | 17.62 | 15.46 |
| 70 | 27.39 | 29.52 | 27.61 | 21.51 | 23.32 | 28.37 | 27.00 | 25.42 | 17.55 | 16.17 | 14.40 | 11.27 | 28.94 | 20.83 |

Blast Only Group (n=14)

| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -20.06 | -19.15 | -20.01 | -18.97 | -18.75 | -18.41 | -17.28 | -18.56 | -17.37 | -19.63 | -19.36 | -19.75 | -19.71 | -20.39 |
| 25 | -20.03 | -18.83 | -19.49 | -18.10 | -19.41 | -20.62 | -16.78 | -18.17 | -17.00 | -19.10 | -19.57 | -19.89 | -20.13 | -19.48 |
| 30 | -19.82 | -19.47 | -19.37 | -18.46 | -19.40 | -19.82 | -18.16 | -17.22 | -17.74 | -19.55 | -20.45 | -20.00 | -19.02 | -19.68 |
| 35 | -17.34 | -18.45 | -20.13 | -19.72 | -19.01 | -19.74 | -16.90 | -17.68 | -16.62 | -18.84 | -19.69 | -19.91 | -19.36 | -20.13 |
| 40 | -18.58 | -14.05 | -19.62 | -14.92 | -16.59 | -17.81 | -18.06 | -14.38 | -12.38 | -18.99 | -17.90 | -19.78 | -20.56 | -20.43 |
| 45 | -15.90 | -8.20 | -18.40 | -8.99 | -10.68 | -17.06 | -16.21 | -8.94 | -7.86 | -20.10 | -12.87 | -19.60 | -19.71 | -19.50 |
| 50 | -10.57 | -1.04 | -17.47 | -2.80 | -4.15 | -16.31 | -17.08 | -2.90 | -2.56 | -17.69 | -4.95 | -20.28 | -12.89 | -10.37 |
| 55 | -1.69 | 4.53 | -17.64 | 2.95 | -1.51 | -13.27 | -10.54 | 3.23 | 2.10 | -8.99 | 1.19 | -20.25 | -3.60 | -0.01 |
| 60 | 5.74 | 9.13 | -9.76 | 6.90 | 0.00 | -5.43 | -3.87 | 3.97 | 5.19 | -0.79 | 3.33 | -12.56 | 5.03 | 6.33 |
| 65 | 12.22 | 10.89 | 0.68 | 4.81 | 8.09 | 0.73 | 4.13 | 10.80 | 12.83 | 6.92 | 8.50 | -2.37 | 11.85 | 11.14 |
| 70 | 17.50 | 20.14 | 6.69 | 22.70 | 19.14 | 1.12 | 8.66 | 22.82 | 19.12 | 11.61 | 20.87 | 5.23 | 13.37 | 21.37 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=4000 Hz

Interrupted Conditioning then Blast Group (n=14)

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2642 | 2644 | 2654 | 2655 | 2656 | 2657 | 2659 | 2660 | 2662 | 2664 | 2665 | 2683 | 2684 | 2685 |
| 20 | -20.36 | -19.13 | -19.53 | -19.78 | -20.33 | -18.72 | -19.67 | -19.74 | -20.22 | -19.66 | -19.56 | -20.05 | -20.13 | -19.03 |
| 25 | -19.82 | -19.22 | -20.29 | -20.16 | -20.22 | -18.33 | -19.22 | -19.74 | -19.15 | -19.31 | -19.27 | -20.33 | -20.56 | -20.40 |
| 30 | -18.83 | -20.07 | -18.71 | -18.76 | -19.88 | -18.25 | -18.50 | -19.35 | -19.98 | -19.69 | -20.12 | -20.52 | -20.86 | -18.96 |
| 35 | -20.08 | -18.29 | -18.63 | -19.46 | -20.09 | -14.15 | -16.69 | -20.35 | -19.04 | -18.66 | -19.07 | -19.81 | -19.12 | -19.16 |
| 40 | -19.75 | -17.43 | -18.16 | -18.46 | -17.94 | -8.63 | -13.87 | -19.06 | -19.56 | -20.12 | -19.24 | -17.99 | -13.28 | -18.09 |
| 45 | -16.24 | -13.73 | -18.22 | -18.55 | -10.47 | -0.90 | -8.56 | -19.28 | -11.68 | -17.09 | -11.86 | -13.99 | -5.88 | -9.12 |
| 50 | -9.96 | -6.35 | -14.63 | -12.15 | -2.07 | 6.05 | -2.17 | -14.03 | -2.95 | -10.22 | -4.88 | -6.04 | 2.19 | -6.22 |
| 55 | -7.50 | -2.18 | -6.02 | -4.93 | 5.24 | 11.91 | 1.57 | -5.85 | 6.04 | -4.18 | 4.04 | 1.14 | 8.27 | 0.20 |
| 60 | -6.70 | -0.29 | 2.39 | 2.21 | 12.05 | 14.88 | 2.61 | 3.08 | 13.30 | 0.14 | 11.11 | 6.42 | 13.13 | 7.24 |
| 65 | 6.22 | 3.23 | 9.23 | 8.59 | 17.61 | 16.41 | 4.18 | 8.17 | 17.82 | 5.68 | 17.89 | 8.72 | 15.69 | 11.76 |
| 70 | 20.23 | 8.44 | 12.19 | 13.43 | 19.68 | 25.74 | 20.29 | 5.74 | 18.12 | 10.95 | 14.66 | 7.61 | 18.40 | 17.90 |

Continuous Conditioning then Blast Group (n=14)

| dB | 2594 | 2595 | 2596 | 2597 | 2598 | 2599 | 2606 | 2607 | 2608 | 2609 | 2610 | 2611 | 2612 | 2613 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -20.59 | -17.58 | -18.72 | -18.22 | -16.94 | -18.79 | -20.05 | -17.34 | -19.16 | -20.31 | -19.06 | -18.56 | -18.58 | -20.24 |
| 25 | -20.66 | -18.27 | -19.44 | -18.35 | -16.77 | -20.88 | -20.21 | -16.47 | -18.78 | -18.22 | -18.41 | -19.57 | -18.48 | -19.96 |
| 30 | -20.24 | -18.20 | -20.55 | -18.30 | -16.21 | -18.47 | -19.53 | -16.99 | -18.19 | -18.79 | -18.15 | -18.91 | -18.29 | -19.41 |
| 35 | -20.23 | -17.16 | -18.84 | -18.37 | -16.47 | -19.78 | -19.94 | -16.97 | -19.06 | -20.77 | -18.34 | -18.00 | -17.85 | -19.45 |
| 40 | -18.97 | -12.81 | -16.26 | -18.33 | -16.39 | -19.80 | -18.76 | -16.88 | -17.34 | -19.65 | -16.78 | -17.28 | -18.08 | -15.67 |
| 45 | -19.81 | -5.84 | -7.99 | -16.11 | -13.00 | -20.00 | -20.97 | -15.92 | -17.15 | -11.83 | -18.16 | -17.37 | -18.15 | -9.26 |
| 50 | -12.50 | 0.32 | -0.66 | -7.83 | -5.74 | -16.27 | -15.20 | -15.56 | -14.06 | -5.09 | -16.12 | -11.18 | -17.89 | -2.67 |
| 55 | -2.96 | 4.61 | 5.72 | 1.11 | 2.09 | -7.71 | -9.60 | -16.20 | -16.83 | 0.89 | -17.06 | -5.32 | -12.71 | 2.73 |
| 60 | 6.01 | 7.08 | 11.93 | 7.72 | 5.40 | 0.70 | -1.07 | -15.22 | -0.61 | 6.94 | -10.34 | -2.62 | -9.62 | 3.52 |
| 65 | 12.87 | 10.93 | 15.35 | 11.51 | 0.69 | 8.50 | 5.52 | -0.48 | 11.19 | 8.22 | -0.90 | -1.61 | -11.59 | 14.85 |
| 70 | 10.31 | 22.91 | 10.72 | 14.68 | 20.62 | 10.05 | 7.98 | 7.76 | 22.69 | 13.83 | 8.92 | 6.37 | 7.12 | 22.21 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=5656 Hz

**Aged Normal Group (n=14)**

Animal #

| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -18.80 | -19.37 | -18.13 | -18.50 | -19.09 | -19.16 | -18.84 | -19.66 | -19.12 | -18.83 | -19.15 | -19.87 | -19.95 | -13.92 |
| 25 | -15.47 | -16.10 | -12.40 | -15.14 | -12.05 | -15.64 | -15.55 | -17.65 | -15.55 | -15.73 | -16.23 | -12.43 | -16.03 | -8.07 |
| 30 | -8.24 | -9.14 | -5.57 | -7.93 | -5.11 | -12.75 | -9.79 | -11.50 | -7.07 | -11.84 | -9.70 | -5.66 | -8.83 | -1.65 |
| 35 | -1.68 | -2.20 | 0.19 | -1.82 | 0.00 | -6.18 | -3.70 | -5.30 | -0.95 | -5.49 | -3.58 | -0.99 | -2.62 | 3.22 |
| 40 | 3.23 | 3.62 | 5.17 | 3.33 | 5.23 | -1.23 | 2.18 | 1.65 | 3.67 | -0.11 | 2.17 | 3.57 | 2.43 | 7.47 |
| 45 | 7.77 | 8.58 | 10.03 | 7.69 | 9.89 | 4.92 | 6.73 | 7.33 | 7.81 | 4.27 | 7.43 | 8.94 | 6.89 | 11.64 |
| 50 | 12.60 | 12.42 | 14.47 | 11.26 | 14.63 | 10.83 | 11.03 | 12.55 | 12.24 | 9.17 | 11.79 | 13.27 | 11.53 | 15.84 |
| 55 | 17.80 | 16.48 | 19.73 | 15.29 | 20.06 | 17.63 | 15.89 | 17.17 | 17.47 | 14.63 | 15.00 | 19.44 | 16.69 | 22.15 |
| 60 | 24.09 | 23.53 | 25.85 | 22.78 | 26.00 | 25.28 | 23.12 | 23.47 | 24.05 | 22.19 | 20.19 | 27.75 | 22.86 | 28.23 |
| 65 | 28.22 | 26.76 | 28.95 | 28.35 | 27.79 | 29.07 | 28.53 | 27.67 | 28.62 | 27.02 | 26.25 | 31.89 | 25.01 | 29.89 |
| 70 | 25.03 | 20.08 | 23.64 | 27.80 | 24.02 | 22.32 | 29.45 | 20.95 | 27.74 | 25.57 | 29.72 | 29.07 | 23.83 | 19.87 |

**Interrupted Conditioning Group (n=14)**

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -19.58 | -19.32 | -17.87 | -16.86 | -18.40 | -20.35 | -19.66 | -19.28 | -19.44 | -18.16 | -20.09 | -17.46 | -19.24 | -20.60 |
| 25 | -18.00 | -18.85 | -14.92 | -16.55 | -14.78 | -19.65 | -16.18 | -16.87 | -18.35 | -15.35 | -17.04 | -13.62 | -19.55 | -16.71 |
| 30 | -16.97 | -19.56 | -7.81 | -9.26 | -9.99 | -16.02 | -10.18 | -9.61 | -17.62 | -9.15 | -13.59 | -8.85 | -16.11 | -10.62 |
| 35 | -11.68 | -18.14 | -3.20 | -4.06 | -4.98 | -10.09 | -6.09 | -4.17 | -14.42 | -5.82 | -7.46 | -3.90 | -10.15 | -5.37 |
| 40 | -5.97 | -18.09 | 1.85 | 0.57 | 0.33 | -7.22 | -1.03 | 1.48 | -8.73 | -1.69 | -2.67 | 0.55 | -5.88 | -0.19 |
| 45 | -1.19 | -7.33 | 6.59 | 4.83 | 5.04 | 0.27 | 3.66 | 5.99 | -4.21 | 2.49 | 1.68 | 5.08 | -0.94 | 4.80 |
| 50 | 4.51 | -0.90 | 10.70 | 9.63 | 9.61 | 4.66 | 7.62 | 10.89 | 3.66 | 6.03 | 6.84 | 9.10 | 3.04 | 9.10 |
| 55 | 8.88 | 6.12 | 13.44 | 15.41 | 14.47 | 10.14 | 12.73 | 15.65 | 13.82 | 10.62 | 12.33 | 14.24 | 9.27 | 13.59 |
| 60 | 16.10 | 17.34 | 17.88 | 22.11 | 22.50 | 16.02 | 21.63 | 23.25 | 23.33 | 19.42 | 21.12 | 21.41 | 20.62 | 21.23 |
| 65 | 26.11 | 26.39 | 24.76 | 24.67 | 27.50 | 24.40 | 28.53 | 28.50 | 25.77 | 20.27 | 26.25 | 19.96 | 27.59 | 23.73 |
| 70 | 25.62 | 27.03 | 20.81 | 19.70 | 20.43 | 13.35 | 28.05 | 22.83 | 13.30 | 21.42 | 29.84 | 25.59 | 29.09 | 16.00 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=5656 Hz

**Continuous Conditioning Group (n=14)**

| | Animal # | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **dB** | **2676** | **2677** | **2678** | **2679** | **2680** | **2681** | **2682** | **2686** | **2687** | **2688** | **2689** | **2690** | **2691** | **2692** |
| **20** | -19.22 | -20.12 | -20.81 | -20.53 | -19.94 | -20.34 | -19.96 | -19.69 | -19.37 | -20.32 | -19.35 | -19.76 | -18.05 | -20.19 |
| **25** | -20.15 | -19.71 | -20.16 | -19.77 | -19.17 | -19.81 | -19.96 | -18.31 | -20.22 | -20.03 | -19.91 | -20.22 | -17.62 | -20.56 |
| **30** | -19.12 | -16.73 | -16.94 | -20.16 | -18.65 | -16.63 | -16.42 | -11.58 | -18.12 | -15.45 | -15.06 | -17.99 | -10.75 | -19.38 |
| **35** | -18.88 | -8.80 | -8.06 | -18.00 | -15.26 | -10.12 | -7.50 | -4.51 | -8.90 | -9.45 | -7.39 | -10.69 | -4.52 | -15.42 |
| **40** | -15.60 | -4.12 | -2.75 | -14.90 | -6.06 | -4.34 | -0.45 | 2.03 | -2.70 | -2.59 | -1.02 | -3.91 | 0.55 | -9.46 |
| **45** | -13.24 | -0.43 | 2.95 | -8.68 | 0.04 | 0.61 | 4.33 | 6.93 | 2.34 | 2.78 | 4.72 | 1.41 | 5.83 | -5.38 |
| **50** | -13.28 | 0.26 | 8.52 | 0.25 | 4.84 | 3.06 | 9.08 | 10.33 | 6.61 | 8.15 | 9.38 | 6.52 | 10.97 | 0.55 |
| **55** | 4.45 | 5.14 | 14.81 | 9.79 | 7.97 | 12.06 | 13.30 | 12.08 | 10.78 | 12.64 | 12.45 | 10.61 | 18.32 | 6.50 |
| **60** | 18.81 | 19.57 | 21.81 | 20.25 | 13.10 | 19.18 | 20.03 | 20.80 | 19.44 | 18.34 | 18.30 | 15.04 | 24.60 | 11.61 |
| **65** | 25.76 | 17.83 | 17.69 | 26.55 | 23.11 | 22.59 | 25.29 | 26.60 | 26.55 | 24.89 | 21.93 | 21.91 | 23.61 | 19.09 |
| **70** | 21.00 | 22.59 | 27.13 | 20.38 | 24.20 | 25.67 | 22.73 | 25.60 | 21.00 | 15.69 | 17.58 | 22.73 | 18.02 | 21.94 |

**Blast Only Group (n=14)**

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **dB** | **2600** | **2601** | **2614** | **2615** | **2616** | **2617** | **2618** | **2619** | **2620** | **2648** | **2658** | **2661** | **2663** | **2666** |
| **20** | -19.99 | -18.68 | -19.81 | -19.09 | -19.73 | -19.41 | -18.21 | -19.44 | -18.76 | -19.59 | -19.48 | -19.73 | -19.05 | -20.45 |
| **25** | -19.25 | -18.80 | -20.77 | -17.69 | -18.77 | -19.00 | -. 90 | -18.97 | -14.96 | -19.07 | -18.92 | -20.34 | -19.47 | -19.68 |
| **30** | -18.94 | -19.83 | -19.53 | -19.17 | -18.94 | -18.83 | -17.29 | -19.25 | -15.46 | -17.15 | -20.31 | -19.09 | -20.05 | -20.23 |
| **35** | -19.76 | -19.68 | -20.41 | -19.61 | -19.47 | -20.41 | -17.81 | -18.33 | -12.36 | -17.34 | -19.81 | -18.23 | -19.02 | -18.77 |
| **40** | -17.50 | -17.83 | -18.84 | -18.66 | -19.92 | -19.96 | -16.89 | -17.77 | -7.44 | -16.42 | -17.15 | -19.36 | -19.89 | -16.69 |
| **45** | -14.24 | -13.52 | -15.80 | -15.80 | -10.21 | -11.96 | -16.53 | -10.12 | -1.51 | -15.02 | -7.68 | -17.56 | -9.80 | -7.35 |
| **50** | -7.99 | -5.83 | -6.88 | -8.48 | -1.51 | -2.62 | -9.95 | -2.36 | 3.15 | -5.60 | -0.30 | -13.77 | -0.09 | -0.51 |
| **55** | -0.14 | 2.82 | 2.09 | 1.61 | 5.84 | 5.64 | -0.76 | 5.33 | 8.76 | 1.94 | 6.07 | -3.25 | 7.28 | 6.11 |
| **60** | 7.34 | 9.94 | 8.81 | 10.00 | 11.83 | 12.84 | 8.31 | 12.44 | 14.12 | 7.95 | 10.61 | 5.08 | 13.77 | 11.03 |
| **65** | 13.91 | 15.13 | 14.53 | 16.14 | 15.94 | 18.34 | 14.90 | 16.97 | 17.98 | 12.06 | 15.97 | 11.25 | 18.15 | 19.58 |
| **70** | 22.91 | 16.66 | 19.34 | 24.37 | 26.90 | 19.67 | 17.35 | 22.32 | 23.61 | 20.75 | 28.12 | 13.18 | 26.71 | 28.13 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=5656 Hz

**Interrupted Conditioning then Blast Group (n=14)**

Animal #

| dB | 2642 | 2644 | 2654 | 2655 | 2656 | 2657 | 2659 | 2660 | 2662 | 2664 | 2665 | 2683 | 2684 | 2685 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -19.69 | -20.87 | -19.18 | -19.71 | -19.97 | -19.34 | -19.43 | -19.30 | -19.80 | -19.73 | -19.25 | -19.14 | -19.32 | -19.76 |
| 25 | -19.83 | -19.12 | -18.95 | -19.44 | -19.89 | -18.87 | -19.37 | -20.10 | -19.48 | -19.21 | -19.66 | -20.52 | -20.09 | -20.35 |
| 30 | -19.30 | -19.18 | -19.62 | -20.06 | -19.38 | -18.84 | -19.91 | -18.66 | -20.60 | -20.37 | -18.75 | -19.56 | -20.15 | -19.77 |
| 35 | -19.11 | -20.08 | -20.70 | -20.29 | -19.59 | -16.19 | -18.63 | -18.60 | -19.49 | -19.41 | -17.84 | -20.64 | -19.65 | -19.69 |
| 40 | -17.88 | -13.37 | -17.58 | -18.66 | -18.54 | -13.57 | -18.20 | -19.29 | -15.61 | -19.69 | -12.75 | -16.57 | -17.89 | -14.20 |
| 45 | -10.98 | -7.54 | -10.93 | -14.54 | -15.40 | -5.38 | -17.27 | -14.05 | -5.79 | -15.52 | -3.71 | -9.65 | -13.37 | -8.93 |
| 50 | -3.52 | 0.80 | -1.15 | -6.85 | -9.93 | 1.85 | -9.61 | -5.07 | 1.46 | -6.42 | 2.81 | -0.73 | -6.46 | -2.00 |
| 55 | 3.62 | 8.08 | 6.01 | 2.71 | 1.30 | 8.37 | 0.81 | 4.05 | 7.35 | 1.13 | 9.02 | 5.82 | 2.75 | 3.69 |
| 60 | 10.12 | 13.89 | 11.53 | 9.58 | 9.34 | 12.83 | 7.86 | 10.69 | 12.12 | 8.22 | 15.64 | 12.61 | 12.98 | 9.75 |
| 65 | 17.46 | 18.24 | 15.99 | 13.44 | 18.97 | 21.02 | 14.39 | 16.07 | 15.02 | 12.79 | 22.73 | 17.91 | 20.20 | 16.11 |
| 70 | 27.29 | 23.20 | 23.37 | 22.29 | 27.69 | 29.83 | 16.70 | 21.92 | 19.72 | 17.88 | 30.95 | 25.20 | 26.91 | 24.35 |

**Continuous Conditioning then Blast Group (n=14)**

| dB | 2594 | 2595 | 2596 | 2597 | 2598 | 2599 | 2606 | 2607 | 2608 | 2609 | 2610 | 2611 | 2612 | 2613 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -20.21 | -17.52 | -19.28 | -18.58 | -16.40 | -19.71 | -19.27 | -17.97 | -19.08 | -20.53 | -21.09 | -19.21 | -20.02 | -19.07 |
| 25 | -19.58 | -19.76 | -19.21 | -21.41 | -18.00 | -19.72 | -19.27 | -17.43 | -17.99 | -20.62 | -20.24 | -19.69 | -19.09 | -19.57 |
| 30 | -21.31 | -17.57 | -20.16 | -19.66 | -16.37 | -17.76 | -18.98 | -18.44 | -18.16 | -19.49 | -19.81 | -18.50 | -19.99 | -20.10 |
| 35 | -19.41 | -20.07 | -19.58 | -19.27 | -18.36 | -18.59 | -17.87 | -16.97 | -16.52 | -18.02 | -20.28 | -18.18 | -20.41 | -15.27 |
| 40 | -17.16 | -17.97 | -20.22 | -14.77 | -13.84 | -17.20 | -18.08 | -18.90 | -12.98 | -17.16 | -19.84 | -20.05 | -18.85 | -7.54 |
| 45 | -10.15 | -13.89 | -13.12 | -6.72 | -4.53 | -13.07 | -17.37 | -16.45 | -5.37 | -10.03 | -13.69 | -16.24 | -17.59 | 1.57 |
| 50 | -1.40 | -5.20 | -5.75 | 1.58 | 1.48 | -3.80 | -9.54 | -12.19 | 2.02 | -2.62 | -4.14 | -12.84 | -10.94 | 8.97 |
| 55 | 6.08 | 1.96 | -0.59 | 8.01 | 7.46 | 3.47 | -0.09 | -5.59 | 8.06 | 2.30 | 4.31 | -3.48 | -0.58 | 15.33 |
| 60 | 11.70 | 8.91 | 13.54 | 13.33 | 12.38 | 9.80 | 8.05 | 3.39 | 13.48 | 8.11 | 10.89 | 3.19 | 5.18 | 21.39 |
| 65 | 18.43 | 14.04 | 26.13 | 18.53 | 15.31 | 13.99 | 13.74 | 11.36 | 16.93 | 14.06 | 13.63 | 9.66 | 10.91 | 27.89 |
| 70 | 29.55 | 21.80 | 32.10 | 24.92 | 22.62 | 24.73 | 17.98 | 16.62 | 26.17 | 18.98 | 23.87 | 12.95 | 16.58 | 29.01 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=8000 Hz

Aged Normal Group (n=14)

Animal #

| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -17.03 | -16.77 | -13.36 | -16.24 | -13.51 | -11.45 | -16.62 | -17.90 | -16.06 | -16.48 | -16.17 | -13.03 | -14.45 | -11.58 |
| 25 | -13.00 | -12.34 | -10.17 | -9.95 | -8.93 | -5.79 | -12.72 | -16.15 | -10.59 | -16.22 | -16.53 | -6.59 | -10.82 | -7.68 |
| 30 | -5.82 | -6.91 | -4.14 | -4.89 | -3.06 | -0.10 | -6.86 | -13.03 | -3.58 | -9.95 | -9.20 | -0.31 | -5.77 | -0.33 |
| 35 | -0.26 | -0.88 | 1.17 | 0.69 | 2.48 | 4.42 | -0.62 | -6.76 | 2.52 | -3.86 | -4.12 | 5.00 | -0.12 | 4.12 |
| 40 | 4.86 | 4.13 | 5.91 | 5.29 | 7.54 | 8.87 | 4.53 | 1.12 | 7.75 | 1.21 | 1.00 | 9.25 | 4.38 | 8.55 |
| 45 | 9.59 | 8.47 | 10.46 | 9.44 | 11.81 | 13.07 | 9.06 | 6.13 | 11.88 | 5.71 | 5.38 | 12.91 | 9.33 | 12.23 |
| 50 | 14.35 | 12.49 | 15,05 | 13.19 | 15.44 | 17.78 | 13.28 | 11.74 | 15.77 | 10.48 | 9.77 | 15.72 | 14.22 | 15.17 |
| 55 | 20.13 | 17.11 | 21.88 | 17.94 | 19.79 | 23.52 | 19.04 | 15.79 | 20.34 | 12.47 | 17.86 | 21.15 | 20.20 | 21.13 |
| 60 | 27.41 | 24.94 | 29.67 | 25.53 | 27.09 | 30.71 | 26.87 | 22.25 | 26.55 | 19.36 | 25.27 | 29.18 | 27.72 | 29.88 |
| 65 | 33.74 | 32.30 | 34.98 | 32.36 | 32.66 | 35.97 | 33.77 | 31.20 | 32.50 | 28.38 | 32.92 | 35.41 | 32.75 | 35.13 |
| 70 | 36.04 | 35.52 | 36.04 | 35.78 | 34.99 | 37.36 | 37.18 | 34.14 | 35.65 | 33.30 | 36.98 | 37.91 | 33.26 | 36.55 |

Interrupted Conditioning Group (n=14)

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -16.10 | -13.61 | -14.36 | -12.07 | -14.78 | -16.22 | -13.18 | -13.03 | -13.84 | -13.03 | -15.58 | -15.68 | -15.12 | -14.80 |
| 25 | -12.61 | -6.82 | -9.72 | -7.88 | -12.07 | -14.60 | -6.66 | -9.83 | -9.93 | -5.63 | -11.88 | -9.53 | -11.78 | -10.51 |
| 30 | -6.52 | -1.22 | -3.51 | -2.62 | -5.80 | -8.87 | -0.80 | -2.81 | -3.37 | 0.68 | -5.74 | -4.22 | -6.90 | -5.24 |
| 35 | -2.33 | 3.84 | 2.33 | 2.81 | 0.13 | -3.19 | 4.75 | 2.27 | 1.46 | 6.12 | -0.67 | 1.32 | -1.98 | 0.33 |
| 40 | 3.02 | 8.31 | 7.17 | 7.08 | 5.52 | 2.25 | 9.40 | 6.83 | 5.53 | 10.42 | 4.18 | 5.70 | 2.66 | 5.34 |
| 45 | 7.83 | 12.35 | 11.42 | 10.89 | 9.90 | 7.12 | 13.31 | 11.19 | 9.67 | 13.75 | 8.05 | 9.72 | 6.99 | 9.77 |
| 50 | 12.36 | 15.60 | 15.23 | 14.30 | 13.93 | 12.08 | 16.57 | 15.55 | 12.70 | 16.00 | 11.68 | 13.70 | 10.66 | 13.89 |
| 55 | 16.02 | 19.53 | 18.37 | 19.29 | 17.10 | 16.10 | 19.81 | 20.70 | 18.22 | 18.31 | 14.74 | 19.73 | 16.78 | 17.25 |
| 60 | 24.63 | 27.75 | 24.23 | 26.39 | 24.17 | 22.61 | 27.53 | 27.48 | 28.14 | 26.22 | 22.78 | 27.30 | 25.95 | 23.75 |
| 65 | 33.52 | 34.46 | 32.30 | 32.38 | 33.09 | 30.92 | 34.52 | 33.22 | 35.00 | 32.97 | 32.04 | 33.04 | 32.60 | 32.67 |
| 70 | 36.68 | 35.93 | 35.16 | 35.97 | 37.07 | 33.11 | 37.17 | 15.48 | 37.26 | 33.95 | 36.64 | 34.80 | 34.91 | 35.96 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=8000 Hz

Continuous Conditioning Group (n=14)

Amplitude #

| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -15.14 | -15.71 | -16.04 | -16.63 | -15.83 | -15.95 | -16.46 | -15.80 | -16.81 | -15.05 | -15.54 | -16.06 | -15.97 | -15.78 |
| 25 | -13.62 | -12.83 | -15.08 | -14.27 | -14.08 | -14.43 | -14.72 | -13.50 | -15.85 | -14.87 | -12.24 | -14.17 | -11.53 | -14.70 |
| 30 | -8.90 | -8.87 | -9.74 | -8.02 | -12.49 | -6.95 | -7.22 | -8.14 | -9.63 | -7.03 | -6.56 | -9.81 | -6.76 | -12.89 |
| 35 | -1.52 | -2.51 | -4.51 | -1.84 | -5.87 | 0.33 | -1.01 | -1.94 | -2.71 | -1.45 | -0.25 | -3.59 | -1.50 | -9.36 |
| 40 | 3.94 | 2.93 | 0.96 | 3.80 | 1.99 | 5.67 | 4.60 | 3.29 | 2.95 | 4.42 | 4.86 | 1.60 | 2.88 | -4.24 |
| 45 | 8.79 | 7.50 | 6.05 | 8.39 | 8.14 | 10.43 | 9.30 | 7.86 | 7.90 | 9.36 | 9.22 | 6.15 | 6.14 | 1.67 |
| 50 | 13.00 | 11.81 | 10.45 | 12.08 | 13.40 | 14.12 | 13.47 | 11.79 | 12.55 | 13.69 | 13.00 | 10.54 | 9.34 | 6.25 |
| 55 | 17.22 | 17.73 | 17.48 | 15.55 | 17.32 | 17.71 | 17.40 | 14.38 | 17.19 | 16.71 | 15.67 | 14.83 | 18.46 | 10.77 |
| 60 | 26.28 | 26.30 | 27.16 | 25.50 | 21.34 | 25.83 | 24.41 | 22.17 | 25.24 | 18.97 | 24.41 | 21.15 | 27.81 | 21.69 |
| 65 | 33.28 | 32.30 | 32.39 | 33.45 | 30.09 | 32.75 | 32.52 | 30.66 | 32.73 | 30.05 | 33.20 | 29.36 | 32.70 | 27.52 |
| 70 | 34.61 | 33.60 | 31.12 | 35.72 | 34.91 | 35.01 | 36.15 | 33.52 | 34.57 | 35.41 | 36.23 | 35.00 | 31.77 | 32.79 |

Blast Only Group (n=14)

| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -16.90 | -16.12 | -16.61 | -16.53 | -17.72 | -16.81 | -14.78 | -15.29 | -14.20 | -15.49 | -15.98 | -16.90 | -16.71 | -16.34 |
| 25 | -16.59 | -16.56 | -16.25 | -16.27 | -17.63 | -16.53 | -14.10 | -14.20 | -14.31 | -15.69 | -16.66 | -17.62 | -16.60 | -16.87 |
| 30 | -15.81 | -15.69 | -15.30 | -15.50 | -16.21 | -17.96 | -14.70 | -14.59 | -14.13 | -15.20 | -15.78 | -17.72 | -15.00 | -15.90 |
| 35 | -16.79 | -16.05 | -13.66 | -14.51 | -10.59 | -16.48 | -15.70 | -13.00 | -14.06 | -11.85 | -13.36 | -16.99 | -11.65 | -11.77 |
| 40 | -15.53 | -15.53 | -11.78 | -10.21 | -6.88 | -12.61 | -14.85 | -7.72 | -10.36 | -8.42 | -9.82 | -16.31 | -8.55 | -7.09 |
| 45 | -17.13 | -9.19 | -7.07 | -7.39 | -5.27 | -6.14 | -10.20 | -1.46 | -2.65 | -3.39 | -6.35 | -12.85 | -4.12 | -5.02 |
| 50 | -15.89 | -0.75 | -0.28 | -12.62 | -9.42 | 2.57 | -2.73 | 3.98 | 3.88 | 0.05 | -4.05 | -3.96 | -4.64 | -2.45 |
| 55 | -1.86 | 7.13 | 4.94 | 6.24 | 11.75 | 9.66 | 4.62 | 7.80 | 8.42 | 4.84 | 1.23 | 3.61 | -0.85 | 12.34 |
| 60 | 12.27 | 13.82 | 6.45 | 20.72 | 24.15 | 14.60 | 11.82 | 13.04 | 11.37 | 14.27 | 19.81 | 10.20 | 19.10 | 24.91 |
| 65 | 23.60 | 20.27 | 17.70 | 30.86 | 31.72 | 17.71 | 17.74 | 26.63 | 24.92 | 23.58 | 29.66 | 16.01 | 29.40 | 31.02 |
| 70 | 29.75 | 28.16 | 31.13 | 35.55 | 34.79 | 28.62 | 26.74 | 34.37 | 32.48 | 29.58 | 31.52 | 27.26 | 33.15 | 32.41 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=8000 Hz

**Interrupted Conditioning then Blast Group (n=14)**

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **dB** | **2642** | **2644** | **2654** | **2655** | **2656** | **2657** | **2659** | **2660** | **2662** | **2664** | **2665** | **2683** | **2684** | **2685** |
| **20** | -14.72 | -16.74 | -17.61 | -15.78 | -17.62 | -14.68 | -16.72 | -16.37 | -15.98 | -16.83 | -14.86 | -16.34 | -14.87 | -15.83 |
| **25** | -15.37 | -16.31 | -16.69 | -15.49 | -16.90 | -14.25 | -15.83 | -16.28 | -16.80 | -16.26 | -11.69 | -15.40 | -14.58 | -14.57 |
| **30** | -12.21 | -16.69 | -15.43 | -15.39 | -15.39 | -11.93 | -16.56 | -16.01 | -15.56 | -15.20 | -4.83 | -15.53 | -10.37 | -13.79 |
| **35** | -8.68 | -14.45 | -11.67 | -15.46 | -9.98 | -8.13 | -16.28 | -15.79 | -14.45 | -15.78 | 0.89 | -11.65 | -5.91 | -9.82 |
| **40** | -7.81 | -7.25 | -7.65 | -8.01 | -5.82 | -5.60 | -15.12 | -11.31 | -8.90 | -9.69 | 5.22 | -8.51 | -2.56 | -5.66 |
| **45** | -4.90 | -3.04 | -4.37 | -2.97 | -2.95 | -4.37 | -7.25 | -5.35 | -3.80 | -3.54 | 9.40 | -7.07 | -1.01 | 0.83 |
| **50** | 3.35 | 2.56 | 3.47 | 0.53 | 2.60 | 2.33 | 0.94 | 0.83 | 1.38 | 2.50 | 12.67 | -1.06 | 4.34 | 5.75 |
| **55** | 15.21 | 5.46 | 11.68 | 3.22 | 10.97 | 16.15 | 7.14 | 6.03 | 2.82 | 8.39 | 17.27 | 7.28 | 14.33 | 12.29 |
| **60** | 24.42 | 8.16 | 22.13 | 9.97 | 21.33 | 26.53 | 12.71 | 5.90 | 12.04 | 14.05 | 25.46 | 19.47 | 25.00 | 19.76 |
| **65** | 31.54 | 29.89 | 30.77 | 25.02 | 29.37 | 32.66 | 16.91 | 19.87 | 28.02 | 21.30 | 31.55 | 29.55 | 32.89 | 30.69 |
| **70** | 35.43 | 34.67 | 35.28 | 31.28 | 32.40 | 33.89 | 28.30 | 32.21 | 35.48 | 31.62 | 33.05 | 34.97 | 35.44 | 34.73 |

**Continuous Conditioning then Blast Group (n=14)**

| **dB** | **2594** | **2595** | **2596** | **2597** | **2598** | **2599** | **2606** | **2607** | **2608** | **2609** | **2610** | **2611** | **2612** | **2613** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **20** | -17.72 | -16.40 | -17.08 | -15.72 | -16.86 | -15.00 | -15.72 | -15.83 | -14.90 | -15.50 | -16.98 | -17.11 | -16.25 | -16.58 |
| **25** | -16.03 | -15.20 | -11.70 | -16.14 | -15.47 | -15.98 | -16.59 | -17.00 | -15.56 | -15.64 | -15.22 | -16.79 | -16.91 | -14.80 |
| **30** | -11.88 | -16.57 | -7.24 | -12.50 | -14.15 | -15.34 | -17.02 | -15.72 | -15.59 | -16.78 | -16.54 | -16.31 | -15.83 | -14.87 |
| **35** | -7.59 | -16.21 | -1.15 | -9.93 | -11.75 | -12.79 | -15.55 | -14.07 | -14.04 | -15.66 | -14.72 | -15.61 | -16.75 | -8.24 |
| **40** | -2.81 | -11.44 | 3.36 | -8.23 | -9.37 | -10.90 | -12.72 | -14.11 | -10.99 | -16.33 | -11.62 | -15.02 | -12.63 | -1.89 |
| **45** | -0.33 | -4.19 | 7.06 | -7.94 | -8.74 | -12.21 | -9.36 | -12.85 | -4.98 | -12.78 | -5.88 | -10.18 | -7.32 | 3.77 |
| **50** | -4.00 | 2.62 | 11.08 | 4.37 | 1.33 | -6.36 | -1.56 | -6.99 | 0.77 | -4.05 | 0.03 | -3.33 | -1.54 | 7.38 |
| **55** | 8.59 | 6.50 | 17.25 | 16.04 | 13.60 | 9.75 | 6.00 | 1.65 | 7.55 | 4.34 | 2.18 | 3.45 | 4.18 | 9.13 |
| **60** | 22.41 | 5.17 | 25.35 | 24.69 | 22.82 | 20.90 | 12.20 | 9.36 | 17.49 | 10.92 | 12.69 | 9.30 | 6.73 | 18.26 |
| **65** | 30.49 | 22.27 | 32.40 | 30.52 | 28.33 | 29.03 | 17.84 | 15.44 | 26.45 | 14.90 | 26.63 | 15.20 | 16.02 | 30.33 |
| **70** | 33.23 | 32.13 | 36.39 | 33.52 | 30.72 | 32.90 | 28.81 | 24.65 | 31.25 | 22.08 | 32.11 | 25.06 | 28.55 | 35.93 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=11312Hz

**Aged Normal Group (n=14)**

Animal #

| dB | 2605 | 2625 | 2626 | 2627 | 2628 | 2629 | 2630 | 2631 | 2632 | 2647 | 2649 | 2673 | 2674 | 2675 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -11.64 | -13.04 | -11.28 | -12.71 | -12.06 | -7.37 | -13.90 | -13.01 | -12.01 | -13.31 | -11.14 | -11.12 | -12.40 | -10.02 |
| 25 | -7.34 | -8.54 | -5.77 | -6.73 | -8.87 | -1.94 | -7.58 | -8.71 | -8.14 | -9.59 | -7.75 | -6.68 | -8.35 | -5.77 |
| 30 | -0.54 | -2.95 | 0.60 | -0.61 | -2.73 | 3.79 | -1.38 | -4.50 | -0.69 | -4.54 | -0.80 | -0.55 | -1.79 | 0.14 |
| 35 | 4.75 | 2.51 | 6.75 | 5.70 | 3.12 | 8.50 | 4.65 | 2.18 | 5.83 | 2.38 | 5.08 | 5.29 | 3.58 | 5.00 |
| 40 | 9.36 | 7.37 | 11.47 | 10.91 | 9.02 | 12.72 | 9.91 | 8.15 | 11.09 | 9.05 | 9.89 | 9.98 | 8.40 | 9.25 |
| 45 | 13.85 | 11.88 | 15.57 | 15.12 | 13.96 | 16.65 | 14.31 | 13.19 | 15.55 | 14.30 | 14.49 | 14.07 | 13.28 | 12.71 |
| 50 | 18.00 | 15.72 | 19.67 | 18.09 | 17.51 | 20.05 | 17.99 | 17.78 | 19.77 | 18.39 | 18.47 | 16.94 | 18.53 | 15.33 |
| 55 | 22.85 | 19.26 | 25.76 | 18.39 | 20.52 | 24.38 | 22.03 | 23.54 | 24.75 | 22.24 | 23.34 | 20.37 | 23.23 | 19.29 |
| 60 | 30.30 | 27.29 | 33.92 | 22.97 | 27.78 | 32.93 | 29.78 | 30.38 | 31.58 | 30.11 | 32.38 | 29.93 | 31.61 | 30.08 |
| 65 | 37.87 | 35.80 | 39.87 | 35.34 | 35.46 | 40.25 | 38.22 | 38.69 | 38.01 | 36.82 | 40.44 | 38.02 | 38.20 | 38.20 |
| 70 | 41.66 | 38.98 | 41.53 | 40.62 | 39.81 | 42.80 | 42.83 | 42.33 | 41.71 | 40.93 | 43.10 | 41.69 | 40.70 | 41.80 |

**Interrupted Conditioning Group (n=14)**

| dB | 2633 | 2634 | 2635 | 2636 | 2637 | 2638 | 2639 | 2640 | 2667 | 2668 | 2669 | 2670 | 2671 | 2672 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -11.45 | -10.00 | -12.01 | -13.05 | -12.88 | -12.16 | -10.05 | -12.56 | -12.26 | -11.80 | -12.13 | -12.46 | -9.20 | -12.48 |
| 25 | -6.45 | -4.72 | -7.68 | -10.10 | -7.56 | -9.09 | -4.26 | -6.31 | -8.96 | -6.98 | -8.84 | -11.05 | -3.99 | -7.14 |
| 30 | -1.28 | 1.19 | -0.69 | -2.63 | -2.79 | -4.65 | 2.32 | -0.04 | -2.70 | 1.19 | -2.21 | -5.53 | 1.51 | -1.04 |
| 35 | 3.74 | 6.13 | 5.75 | 5.17 | 3.15 | 1.12 | 8.37 | 6.03 | 3.46 | 7.78 | 3.07 | 1.64 | 6.69 | 5.58 |
| 40 | 9.10 | 10.72 | 10.80 | 10.81 | 8.42 | 6.60 | 13.54 | 11.00 | 8.53 | 12.79 | 8.98 | 7.84 | 10.66 | 10.62 |
| 45 | 13.35 | 14.54 | 15.57 | 14.85 | 13.10 | 11.44 | 17.85 | 15.47 | 13.06 | 17.29 | 12.54 | 12.56 | 14.38 | 15.11 |
| 50 | 17.68 | 17.60 | 19.02 | 17.79 | 17.02 | 15.95 | 21.35 | 19.11 | 17.65 | 20.48 | 16.40 | 16.77 | 17.27 | 19.00 |
| 55 | 22.13 | 20.23 | 21.47 | 20.63 | 19.80 | 19.32 | 23.14 | 23.02 | 20.36 | 20.87 | 19.01 | 20.80 | 18.76 | 21.13 |
| 60 | 30.62 | 28.79 | 29.39 | 28.25 | 27.03 | 26.64 | 29.53 | 29.58 | 29.62 | 26.35 | 29.87 | 29.96 | 25.11 | 24.02 |
| 65 | 37.83 | 37.81 | 37.79 | 36.80 | 36.10 | 34.14 | 38.55 | 37.68 | 37.27 | 36.55 | 35.58 | 36.16 | 35.61 | 35.56 |
| 70 | 41.36 | 42.01 | 42.44 | 41.58 | 39.98 | 39.50 | 43.33 | 42.32 | 42.05 | 39.19 | 41.89 | 40.22 | 41.44 | 41.67 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=11312Hz

Continuous Conditioning Group (n=14)

| | Animal # | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| dB | 2676 | 2677 | 2678 | 2679 | 2680 | 2681 | 2682 | 2686 | 2687 | 2688 | 2689 | 2690 | 2691 | 2692 |
| 20 | -12.68 | -12.55 | -11.84 | -13.36 | -12.62 | -13.54 | -11.50 | -13.96 | -12.32 | -13.18 | -14.61 | -12.42 | -12.11 | -13.14 |
| 25 | -11.11 | -8.51 | -5.71 | -12.38 | -11.94 | -9.98 | -7.79 | -9.40 | -7.93 | -9.76 | -9.96 | -9.68 | -8.60 | -11.84 |
| 30 | -3.59 | -2.95 | -0.66 | -4.91 | -4.76 | -3.11 | -2.24 | -2.28 | -1.60 | -1.99 | -5.34 | -2.43 | -1.05 | -9.51 |
| 35 | 3.18 | 2.90 | 4.94 | 1.54 | 1.56 | 3.65 | 2.90 | 4.21 | 3.74 | 3.32 | 2.03 | 3.15 | 4.99 | -2.38 |
| 40 | 8.71 | 7.92 | 9.56 | 7.34 | 7.68 | 9.67 | 8.06 | 9.65 | 9.34 | 9.09 | 7.96 | 8.38 | 9.55 | 1.46 |
| 45 | 13.42 | 12.45 | 14.02 | 12.26 | 13.16 | 14.47 | 12.55 | 14.57 | 13.82 | 13.92 | 12.56 | 12.74 | 13.63 | 7.74 |
| 50 | 17.48 | 16.20 | 17.51 | 16.43 | 17.62 | 18.55 | 16.83 | 18.82 | 17.51 | 18.15 | 16.03 | 16.32 | 15.77 | 11.70 |
| 55 | 21.80 | 21.56 | 22.66 | 19.67 | 20.91 | 21.79 | 22.38 | 20.83 | 20.89 | 20.79 | 17.14 | 18.75 | 16.22 | 17.07 |
| 60 | 30.12 | 30.82 | 32.07 | 27.32 | 26.04 | 28.68 | 30.26 | 22.97 | 29.11 | 21.64 | 23.20 | 23.44 | 28.47 | 26.14 |
| 65 | 38.23 | 37.66 | 38.12 | 36.91 | 35.29 | 37.33 | 37.49 | 36.24 | 38.05 | 33.75 | 35.97 | 33.13 | 37.20 | 30.39 |
| 70 | 41.37 | 39.90 | 40.47 | 41.40 | 40.83 | 41.10 | 41.25 | 40.69 | 41.97 | 40.51 | 42.27 | 39.80 | 40.63 | 37.73 |

Blast Only Group (n=14)

| dB | 2600 | 2601 | 2614 | 2615 | 2616 | 2617 | 2618 | 2619 | 2620 | 2648 | 2658 | 2661 | 2663 | 2666 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | -12.83 | -12.96 | -13.47 | -13.86 | -13.55 | -11.87 | -12.14 | -9.39 | -13.25 | -13.49 | -8.93 | -12.85 | -13.93 | -10.35 |
| 25 | -10.24 | -9.29 | -9.85 | -9.82 | -12.09 | -6.29 | -9.78 | -3.87 | -12.12 | -12.84 | -3.65 | -13.50 | -8.89 | -4.57 |
| 30 | -3.97 | -4.16 | -3.37 | -4.27 | -4.38 | -0.43 | -6.81 | 1.70 | -9.17 | -8.24 | 1.85 | -12.03 | -2.08 | 2.53 |
| 35 | 2.25 | 0.07 | 2.79 | 2.16 | 0.40 | 3.94 | -3.39 | 6.77 | -4.71 | -0.73 | 6.67 | -10.73 | 5.28 | 6.66 |
| 40 | 6.89 | 4.76 | 8.00 | 7.67 | 5.88 | 7.87 | -0.35 | 10.61 | -0.71 | 4.40 | 10.94 | -7.62 | 11.02 | 10.61 |
| 45 | 10.42 | 8.24 | 12.58 | 12.17 | 11.06 | 11.63 | 3.11 | 13.46 | 3.58 | 9.19 | 14.78 | -3.94 | 15.90 | 13.94 |
| 50 | 12.91 | 11.92 | 16.23 | 16.21 | 15.81 | 14.91 | 10.79 | 14.59 | 10.44 | 12.95 | 18.26 | -2.76 | 19.86 | 17.39 |
| 55 | 17.39 | 21.51 | 19.28 | 21.91 | 21.97 | 21.13 | 22.03 | 15.64 | 18.98 | 16.91 | 23.30 | 5.58 | 22.62 | 24.23 |
| 60 | 27.54 | 32.33 | 25.72 | 29.94 | 30.84 | 30.10 | 31.70 | 27.79 | 29.39 | 23.70 | 30.86 | 24.39 | 27.41 | 32.81 |
| 65 | 36.54 | 38.83 | 34.41 | 37.67 | 37.66 | 36.88 | 38.80 | 37.30 | 36.45 | 32.45 | 37.04 | 35.51 | 36.37 | 38.00 |
| 70 | 40.89 | 39.22 | 40.04 | 41.87 | 39.86 | 39.84 | 41.43 | 41.32 | 39.10 | 38.18 | 39.12 | 39.72 | 40.25 | 38.64 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$f_2$=11312Hz

**Interrupted Conditioning then Blast Group (n=14)**

| | Animal # | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **dB** | **2642** | **2644** | **2654** | **2655** | **2656** | **2657** | **2659** | **2660** | **2662** | **2664** | **2665** | **2683** | **2684** | **2685** |
| **20** | -12.46 | -12.86 | -12.53 | -11.18 | -12.88 | -12.62 | -12.41 | -12.73 | -14.25 | -12.62 | -11.42 | -9.98 | -11.89 | -12.81 |
| **25** | -12.52 | -8.76 | -11.79 | -3.05 | -8.84 | -9.84 | -9.71 | -9.96 | -8.08 | -9.75 | -6.97 | -4.75 | -6.68 | -10.99 |
| **30** | -7.51 | -0.42 | -8.50 | 3.36 | -1.90 | -3.50 | -3.47 | -1.44 | -0.32 | -6.99 | -1.58 | 1.25 | -1.34 | -5.97 |
| **35** | -2.25 | 6.00 | -0.18 | 8.44 | 4.19 | 1.59 | 1.39 | 5.33 | 5.61 | -0.55 | 3.81 | 6.08 | 3.64 | 0.37 |
| **40** | 3.47 | 11.67 | 4.63 | 12.68 | 9.79 | 7.52 | 5.05 | 11.38 | 11.00 | 4.93 | 8.55 | 10.44 | 8.01 | 7.45 |
| **45** | 8.52 | 16.46 | 10.17 | 16.26 | 14.46 | 12.27 | 9.25 | 16.19 | 15.66 | 10.68 | 13.24 | 14.59 | 12.49 | 9.78 |
| **50** | 13.26 | 20.25 | 13.96 | 19.00 | 18.40 | 16.08 | 12.13 | 20.26 | 19.60 | 13.49 | 16.67 | 18.84 | 16.91 | 15.43 |
| **55** | 18.01 | 22.22 | 18.09 | 22.33 | 21.84 | 21.32 | 15.39 | 22.91 | 22.36 | 19.35 | 21.39 | 23.37 | 22.53 | 20.55 |
| **60** | 26.09 | 28.52 | 28.74 | 30.27 | 29.98 | 31.28 | 27.38 | 26.45 | 29.94 | 27.91 | 30.22 | 30.18 | 30.66 | 26.91 |
| **65** | 34.54 | 37.81 | 37.48 | 37.50 | 38.67 | 38.22 | 35.33 | 33.39 | 36.84 | 36.30 | 37.81 | 37.31 | 37.68 | 35.00 |
| **70** | 39.37 | 42.54 | 40.47 | 41.24 | 43.97 | 40.19 | 39.02 | 39.83 | 43.12 | 40.77 | 41.47 | 41.50 | 40.27 | 39.90 |

**Continuous Conditioning then Blast Group (n=14)**

| **dB** | **2594** | **2595** | **2596** | **2597** | **2598** | **2599** | **2606** | **2607** | **2608** | **2609** | **2610** | **2611** | **2612** | **2613** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **20** | -10.90 | -14.78 | -11.68 | -14.14 | -10.12 | -13.88 | -14.80 | -14.15 | -13.59 | -12.12 | -12.19 | -10.93 | -12.63 | -13.52 |
| **25** | -4.52 | -10.54 | -7.71 | -10.32 | -8.19 | -9.85 | -13.14 | -14.38 | -9.65 | -10.52 | -7.60 | -8.58 | -12.51 | -13.39 |
| **30** | 2.21 | -7.60 | -2.78 | -3.76 | -2.03 | -2.56 | -12.89 | -13.37 | -6.36 | -6.03 | -1.06 | -5.42 | -11.32 | -9.49 |
| **35** | 8.11 | -0.26 | 2.77 | 1.22 | 4.47 | 3.34 | -8.62 | -9.74 | -1.17 | -1.42 | 4.53 | -2.07 | -5.45 | -2.01 |
| **40** | 12.63 | 4.83 | 7.34 | 6.63 | 9.75 | 8.73 | -4.88 | -7.51 | 3.16 | 4.95 | 8.92 | -0.59 | -1.81 | 4.84 |
| **45** | 16.09 | 9.48 | 11.86 | 11.14 | 14.42 | 13.09 | -2.38 | -6.68 | 7.46 | 9.83 | 12.60 | 3.51 | 3.55 | 10.66 |
| **50** | 18.84 | 12.72 | 16.14 | 15.99 | 19.39 | 17.28 | -8.51 | -10.21 | 13.20 | 13.88 | 14.32 | 6.95 | 10.65 | 15.41 |
| **55** | 23.43 | 17.84 | 21.27 | 22.82 | 25.49 | 22.99 | 13.80 | 12.05 | 20.86 | 12.75 | 18.29 | 20.14 | 19.65 | 18.45 |
| **60** | 31.60 | 27.05 | 28.75 | 30.88 | 31.94 | 30.88 | 27.97 | 25.80 | 29.23 | 21.12 | 29.64 | 30.75 | 27.90 | 21.18 |
| **65** | 38.83 | 34.30 | 36.80 | 36.91 | 36.82 | 37.37 | 37.14 | 34.88 | 35.83 | 33.49 | 36.20 | 38.05 | 33.57 | 34.12 |
| **70** | 41.44 | 37.05 | 41.14 | 39.14 | 37.50 | 39.54 | 39.61 | 38.57 | 38.33 | 40.22 | 37.00 | 40.64 | 36.79 | 42.09 |

## APPENDIX B

## MEAN DPOAE AMPLITUDE DATA

**Table 16a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=707 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -7.20 ± 0.15 | -6.86 ± 0.15 | -6.84 ± 0.15 |
| 25 | -6.95 ± 0.16 | -6.85 ± 0.15 | -6.84 ± 0.12 |
| 30 | -6.44 ± 0.25 | -6.68 ± 0.19 | -6.96 ± 0.15 |
| 35 | -5.54 ± 0.47 | -5.98 ± 0.30 | -6.82 ± 0.18 |
| 40 | -1.63 ± 0.64 | -2.36 ± 0.62 | -6.64 ± 0.14 |
| 45 | 3.03 ± 0.82 | 2.74 ± 0.65 | -4.53 ± 0.42 |
| 50 | 4.81 ± 1.05 | 7.67 ± 0.86 | 0.29 ± 0.67 |
| 55 | 5.18 ± 1.07 | 11.70 ± 0.96 | 4.26 ± 0.92 |
| 60 | 15.77 ± 1.46 | 13.30 ± 1.43 | 8.36 ± 0.74 |
| 65 | 26.32 ± 0.75 | 20.97 ± 0.76 | 19.80 ± 0.35 |
| 70 | 31.88 ± 0.66 | 26.27 ± 1.15 | 27.66 ± 0.64 |

**Table 16b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=707 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -7.04 ± 0.12 | -7.31 ± 0.10 | -6.94 ± 0.20 |
| 25 | -6.66 ± 0.12 | -6.90 ± 0.13 | -6.57 ± 0.21 |
| 30 | -7.03 ± 0.18 | -6.92 ± 0.12 | -6.34 ± 0.42 |
| 35 | -6.88 ± 0.18 | -6.85 ± 0.17 | -6.38 ± 0.33 |
| 40 | -6.02 ± 0.20 | -6.63 ± 0.18 | -5.87 ± 0.32 |
| 45 | -3.36 ± 0.87 | -4.47 ± 0.67 | -3.59 ± 0.70 |
| 50 | 1.74 ± 1.03 | -0.49 ± 1.18 | 1.59 ± 0.93 |
| 55 | 7.00 ± 1.28 | 4.27 ± 1.30 | 7.06 ± 0.85 |
| 60 | 13.12 ± 1.46 | 9.37 ± 1.44 | 11.76 ± 0.95 |
| 65 | 20.10 ± 0.89 | 15.95 ± 1.69 | 15.83 ± 1.19 |
| 70 | 19.66 ± 1.04 | 17.74 ± 1.70 | 14.47 ± 1.55 |



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 17a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=1000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -9.57 ± 0.19 | -9.31 ± 0.14 | -9.86 ± 0.17 |
| 25 | -9.61 ± 0.26 | -9.25 ± 0.21 | -9.76 ± 0.16 |
| 30 | -9.73 ± 0.28 | -9.34 ± 0.19 | -9.83 ± 0.10 |
| 35 | -8.28 ± 0.39 | -8.68 ± 0.34 | -9.93 ± 0.14 |
| 40 | -4.74 ± 0.74 | -6.76 ± 0.69 | -9.88 ± 0.14 |
| 45 | 0.35 ± 0.87 | -1.40 ± 0.97 | -8.53 ± 0.28 |
| 50 | 3.52 ± 0.84 | 5.32 ± 1.15 | -4.03 ± 0.58 |
| 55 | 1.94 ± 1.07 | 11.32 ± 0.83 | 4.18 ± 0.65 |
| 60 | 10.37 ± 1.73 | 15.43 ± 0.54 | 11.29 ± 0.60 |
| 65 | 23.10 ± 1.03 | 17.84 ± 0.62 | 16.77 ± 0.71 |
| 70 | 29.17 ± 0.78 | 21.03 ± 1.02 | 22.26 ± 0.74 |

**Table 17b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=1000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -9.94 ± 0.20 | -9.61 ± 0.12 | -9.39 ± 0.26 |
| 25 | -9.83 ± 0.26 | -9.70 ± 0.19 | -9.37 ± 0.32 |
| 30 | -9.57 ± 0.18 | -9.58 ± 0.12 | -9.29 ± 0.21 |
| 35 | -9.27 ± 0.21 | -9.21 ± 0.16 | -9.27 ± 0.21 |
| 40 | -9.46 ± 0.17 | -9.43 ± 0.23 | -9.55 ± 0.30 |
| 45 | -8.62 ± 0.35 | -9.07 ± 0.25 | -8.55 ± 0.38 |
| 50 | -6.07 ± 0.65 | -6.06 ± 0.83 | -5.69 ± 0.87 |
| 55 | -0.14 ± 1.09 | -1.28 ± 1.23 | -0.15 ± 1.10 |
| 60 | 6.09 ± 1.28 | 4.71 ± 1.45 | 6.08 ± 1.00 |
| 65 | 11.62 ± 1.69 | 10.21 ± 1.70 | 11.42 ± 1.06 |
| 70 | 18.27 ± 1.29 | 16.15 ± 1.69 | 16.83 ± 1.27 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 18a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=1414 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -12.00 ± 0.22 | -11.78 ± 0.25 | -12.16 ± 0.15 |
| 25 | -11.99 ± 0.24 | -11.55 ± 0.25 | -12.14 ± 0.12 |
| 30 | -11.64 ± 0.31 | -11.24 ± 0.30 | -11.91 ± 0.20 |
| 35 | -10.48 ± 0.28 | -11.48 ± 0.38 | -11.40 ± 0.24 |
| 40 | -5.40 ± 0.64 | -10.41 ± 0.55 | -11.67 ± 0.32 |
| 45 | -0.03 ± 0.86 | -7.79 ± 1.18 | -11.41 ± 0.24 |
| 50 | 3.46 ± 0.96 | -2.43 ± 1.80 | -8.96 ± 0.94 |
| 55 | 5.36 ± 1.18 | 3.26 ± 2.25 | -2.40 ± 1.58 |
| 60 | 11.35 ± 0.85 | 9.23 ± 2.01 | 5.82 ± 1.85 |
| 65 | 22.77 ± 0.56 | 15.29 ± 1.12 | 12.41 ± 1.69 |
| 70 | 29.54 ± 0.61 | 22.48 ± 1.32 | 15.77 ± 0.88 |

**Table 18b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=1414 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -11.95 ± 0.20 | -12.27 ± 0.11 | -11.63 ± 0.24 |
| 25 | -11.73 ± 0.22 | -12.03 ± 0.17 | -11.47 ± 0.32 |
| 30 | -11.61 ± 0.26 | -11.76 ± 0.11 | -11.39 ± 0.21 |
| 35 | -11.43 ± 0.28 | -11.66 ± 0.15 | -10.92 ± 0.25 |
| 40 | -11.39 ± 0.31 | -11.76 ± 0.17 | -10.57 ± 0.26 |
| 45 | -10.15 ± 0.51 | -11.04 ± 0.21 | -10.57 ± 0.28 |
| 50 | -7.76 ± 0.81 | -10.21 ± 0.59 | -7.87 ± 0.80 |
| 55 | -1.49 ± 1.00 | -5.94 ± 1.17 | -3.55 ± 1.23 |
| 60 | 4.52 ± 0.99 | -0.68 ± 1.61 | 1.37 ± 1.54 |
| 65 | 10.14 ± 0.92 | 5.35 ± 1.49 | 7.60 ± 1.46 |
| 70 | 16.84 ± 1.54 | 11.49 ± 1.32 | 13.73 ± 1.70 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 19a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=2000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -14.18 ± 0.23 | -13.64 ± 0.20 | -14.34 ± 0.15 |
| 25 | -14.36 ± 0.14 | -13.93 ± 0.23 | -14.11 ± 0.21 |
| 30 | -13.82 ± 0.22 | -13.96 ± 0.23 | -14.52 ± 0.21 |
| 35 | -12.51 ± 0.43 | -13.73 ± 0.30 | -14.21 ± 0.17 |
| 40 | -7.39 ± 0.65 | -13.92 ± 0.29 | -14.19 ± 0.15 |
| 45 | -1.25 ± 0.57 | -12.53 ± 0.57 | -13.89 ± 0.25 |
| 50 | 3.34 ± 0.52 | -10.25 ± 1.16 | -13.74 ± 0.32 |
| 55 | 7.23 ± 0.55 | -4.00 ± 1.52 | -10.97 ± 0.71 |
| 60 | 11.64 ± 0.70 | 3.30 ± 1.60 | -2.26 ± 1.22 |
| 65 | 18.32 ± 0.92 | 10.44 ± 1.67 | 7.78 ± 1.42 |
| 70 | 27.38 ± 0.56 | 18.55 ± 1.23 | 17.12 ± 0.92 |

**Table 19b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=2000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -13.93 ± 0.18 | -14.40 ± 0.12 | -13.96 ± 0.23 |
| 25 | -13.55 ± 0.24 | -14.35 ± 0.12 | -13.64 ± 0.23 |
| 30 | -14.29 ± 0.18 | -14.41 ± 0.12 | -13.48 ± 0.24 |
| 35 | -13.65 ± 0.27 | -14.19 ± 0.20 | -13.57 ± 0.22 |
| 40 | -13.33 ± 0.37 | -14.26 ± 0.15 | -13.31 ± 0.28 |
| 45 | -13.32 ± 0.36 | -13.87 ± 0.20 | -13.06 ± 0.28 |
| 50 | -11.26 ± 0.73 | -13.12 ± 0.62 | -11.51 ± 0.56 |
| 55 | -6.19 ± 1.19 | -10.12 ± 1.13 | -8.46 ± 1.50 |
| 60 | 0.35 ± 1.51 | -4.55 ± 1.48 | -2.83 ± 1.94 |
| 65 | 6.18 ± 1.70 | 1.70 ± 1.88 | 2.36 ± 2.32 |
| 70 | 11.95 ± 1.56 | 7.20 ± 1.58 | 8.50 ± 1.96 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 20a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=2828 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -17.18 ± 0.20 | -16.93 ± 0.16 | -17.11 ± 0.15 |
| 25 | -17.00 ± 0.21 | -16.59 ± 0.17 | -17.24 ± 0.12 |
| 30 | -16.01 ± 0.40 | -16.51 ± 0.18 | -16.61 ± 0.16 |
| 35 | -13.09 ± 0.59 | -16.44 ± 0.16 | -17.09 ± 0.15 |
| 40 | -7.85 ± 0.63 | -15.94 ± 0.46 | -17.12 ± 0.22 |
| 45 | -4.00 ± 0.76 | -14.90 ± 0.98 | -16.63 ± 0.29 |
| 50 | 1.46 ± 0.81 | -11.51 ± 1.53 | -14.93 ± 0.67 |
| 55 | 7.36 ± 0.83 | -5.29 ± 1.70 | -9.18 ± 1.23 |
| 60 | 14.88 ± 0.84 | 1.68 ± 1.74 | -0.15 ± 1.53 |
| 65 | 21.73 ± 0.74 | 8.56 ± 1.48 | 9.69 ± 1.64 |
| 70 | 23.31 ± 1.34 | 15.20 ± 1.16 | 19.29 ± 1.62 |

**Table 20b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=2828 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -16.79 ± 0.19 | -16.99 ± 0.14 | -16.74 ± 0.22 |
| 25 | -16.97 ± 0.21 | -17.09 ± 0.14 | -16.62 ± 0.24 |
| 30 | -16.90 ± 0.27 | -16.68 ± 0.13 | -16.80 ± 0.33 |
| 35 | -16.53 ± 0.25 | -16.63 ± 0.12 | -16.46 ± 0.27 |
| 40 | -16.93 ± 0.26 | -16.71 ± 0.16 | -16.36 ± 0.26 |
| 45 | -16.00 ± 0.32 | -15.87 ± 0.33 | -15.91 ± 0.27 |
| 50 | -13.82 ± 0.95 | -13.49 ± 0.90 | -14.05 ± 0.78 |
| 55 | -8.76 ± 1.62 | -8.03 ± 1.39 | -10.35 ± 1.32 |
| 60 | -2.90 ± 1.98 | -2.82 ± 1.84 | -4.78 ± 1.54 |
| 65 | 1.09 ± 1.88 | 3.51 ± 1.53 | 2.36 ± 1.66 |
| 70 | 5.81 ± 1.48 | 10.69 ± 1.24 | 11.06 ± 1.35 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 21a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=4000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -19.45 ± 0.19 | -19.70 ± 0.19 | -19.83 ± 0.13 |
| 25 | -18.08 ± 0.45 | -19.18 ± 0.22 | -19.90 ± 0.15 |
| 30 | -14.09 ± 0.77 | -19.59 ± 0.25 | -19.97 ± 0.21 |
| 35 | -7.65 ± 0.64 | -18.96 ± 0.27 | -19.13 ± 0.43 |
| 40 | -2.25 ± 0.56 | -17.26 ± 0.61 | -16.74 ± 0.93 |
| 45 | 2.69 ± 0.48 | -13.91 ± 1.22 | -12.53 ± 1.26 |
| 50 | 7.99 ± 0.45 | -6.20 ± 1.17 | -6.90 ± 1.38 |
| 55 | 13.59 ± 0.70 | 3.36 ± 1.10 | 1.47 ± 1.38 |
| 60 | 20.75 ± 0.60 | 12.65 ± 1.07 | 13.01 ± 0.99 |
| 65 | 23.31 ± 1.04 | 18.53 ± 0.77 | 18.72 ± 0.86 |
| 70 | 22.25 ± 1.48 | 21.64 ± 1.10 | 22.81 ± 1.60 |

**Table 21b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=4000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -19.10 ± 0.25 | -19.71 ± 0.13 | -18.87 ± 0.30 |
| 25 | -19.04 ± 0.31 | -19.72 ± 0.17 | -18.89 ± 0.35 |
| 30 | -19.15 ± 0.25 | -19.46 ± 0.22 | -18.59 ± 0.31 |
| 35 | -18.82 ± 0.33 | -18.76 ± 0.43 | -18.66 ± 0.35 |
| 40 | -17.43 ± 0.69 | -17.26 ± 0.85 | -17.36 ± 0.49 |
| 45 | -14.57 ± 1.28 | -12.54 ± 1.42 | -15.11 ± 1.28 |
| 50 | -10.08 ± 1.84 | -5.96 ± 1.60 | -10.03 ± 1.68 |
| 55 | -4.54 ± 2.18 | 0.55 ± 1.60 | -5.09 ± 2.21 |
| 60 | 0.94 ± 1.77 | 5.83 ± 1.71 | 0.70 ± 2.11 |
| 65 | 7.23 ± 1.31 | 10.80 ± 1.42 | 6.08 ± 2.09 |
| 70 | 15.02 ± 1.92 | 15.24 ± 1.54 | 13.30 ± 1.67 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 22a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=5656 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -18.74 ± 0.39 | -19.02 ± 0.30 | -19.83 ± 0.19 |
| 25 | -14.57 ± 0.66 | -16.89 ± 0.49 | -19.69 ± 0.22 |
| 30 | -8.20 ± 0.81 | -12.52 ± 1.06 | -16.64 ± 0.74 |
| 35 | -2.22 ± 0.68 | -7.82 ± 1.20 | -10.54 ± 1.23 |
| 40 | 3.03 ± 0.58 | -3.34 ± 1.46 | -4.67 ± 1.42 |
| 45 | 7.85 ± 0.52 | 1.91 ± 1.10 | 0.30 ± 1.53 |
| 50 | 12.40 ± 0.46 | 6.75 ± 0.92 | 4.66 ± 1.70 |
| 55 | 17.53 ± 0.58 | 12.19 ± 0.75 | 10.78 ± 1.02 |
| 60 | 24.24 ± 0.58 | 20.28 ± 0.67 | 18.63 ± 0.91 |
| 65 | 28.14 ± 0.44 | 25.32 ± 0.71 | 23.10 ± 0.84 |
| 70 | 24.94 ± 0.92 | 22.36 ± 1.47 | 21.88 ± 0.87 |

**Table 22b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=5656 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -19.39 ± 0.16 | -19.61 ± 0.12 | -19.14 ± 0.33 |
| 25 | -18.83 ± 0.37 | -19.63 ± 0.14 | -19.40 ± 0.28 |
| 30 | -18.86 ± 0.36 | -19.58 ± 0.16 | -19.02 ± 0.35 |
| 35 | -18.64 ± 0.54 | -19.28 ± 0.32 | -18.49 ± 0.40 |
| 40 | -17.45 ± 0.84 | -16.70 ± 0.63 | -16.75 ± 0.93 |
| 45 | -11.94 ± 1.19 | -10.93 ± 1.14 | -11.19 ± 1.51 |
| 50 | -4.48 ± 1.24 | -3.20 ± 1.14 | -3.88 ± 1.66 |
| 55 | 3.52 ± 0.92 | 4.62 ± 0.75 | 3.33 ± 1.46 |
| 60 | 10.29 ± 0.70 | 11.23 ± 0.60 | 10.24 ± 1.28 |
| 65 | 15.78 ± 0.64 | 17.17 ± 0.77 | 16.04 ± 1.42 |
| 70 | 22.14 ± 1.22 | 24.09 ± 1.13 | 22.85 ± 1.51 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 23a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=8000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -15.05 ± 0.56 | -14.39 ± 0.35 | -15.91 ± 0.13 |
| 25 | -11.25 ± 0.93 | -9.96 ± 0.68 | -13.99 ± 0.31 |
| 30 | -5.28 ± 1.02 | -4.07 ± 0.70 | -8.79 ± 0.54 |
| 35 | 0.27 ± 0.92 | 1.23 ± 0.73 | -2.70 ± 0.67 |
| 40 | 5.31 ± 0.76 | 5.96 ± 0.66 | 2.83 ± 0.65 |
| 45 | 9.68 ± 0.69 | 10.14 ± 0.58 | 7.64 ± 0.58 |
| 50 | 13.89 ± 0.59 | 13.88 ± 0.48 | 11.82 ± 0.56 |
| 55 | 19.17 ± 0.75 | 18.00 ± 0.46 | 16.32 ± 0.53 |
| 60 | 26.60 ± 0.82 | 25.64 ± 0.51 | 24.16 ± 0.71 |
| 65 | 33.15 ± 0.52 | 33.05 ± 0.29 | 31.64 ± 0.48 |
| 70 | 35.76 ± 0.39 | 35.72 ± 0.33 | 34.32 ± 0.42 |

**Table 23b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=8000 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -16.17 ± 0.25 | -16.07 ± 0.27 | -16.26 ± 0.23 |
| 25 | -16.13 ± 0.31 | -15.46 ± 0.37 | -15.65 ± 0.35 |
| 30 | -15.68 ± 0.29 | -13.92 ± 0.86 | -14.74 ± 0.71 |
| 35 | -14.03 ± 0.57 | -11.23 ± 1.29 | -12.43 ± 1.17 |
| 40 | -11.12 ± 0.89 | -7.05 ± 1.23 | -9.62 ± 1.48 |
| 45 | -7.02 ± 1.13 | -2.89 ± 1.10 | -6.14 ± 1.62 |
| 50 | -3.31 ± 1.58 | 3.01 ± 0.87 | -0.02 ± 1.37 |
| 55 | 5.71 ± 1.14 | 9.87 ± 1.28 | 7.87 ± 1.32 |
| 60 | 15.47 ± 1.45 | 17.64 ± 1.87 | 15.59 ± 1.85 |
| 65 | 24.34 ± 1.52 | 27.86 ± 1.36 | 23.99 ± 1.80 |
| 70 | 31.11 ± 0.76 | 33.48 ± 0.57 | 30.52 ± 1.13 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

**Table 24a.** Mean DPOAE amplitude data (in dB SPL) for the Aged Normal, Interrupted Conditioning, and Continuous Conditioning Groups when $f_2$=11312 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Aged Normal | Interrupted Conditioning | Continuous Conditioning |
|---|---|---|---|
| 20 | -11.79 ± 0.44 | -11.75 ± 0.31 | -12.85 ± 0.23 |
| 25 | -7.27 ± 0.51 | -7.37 ± 0.57 | -9.61 ± 0.49 |
| 30 | -1.18 ± 0.57 | -1.24 ± 0.63 | -3.32 ± 0.61 |
| 35 | 4.67 ± 0.48 | 4.83 ± 0.59 | 2.84 ± 0.49 |
| 40 | 9.76 ± 0.38 | 10.03 ± 0.51 | 8.17 ± 0.56 |
| 45 | 14.21 ± 0.33 | 14.37 ± 0.49 | 12.95 ± 0.45 |
| 50 | 18.02 ± 0.37 | 18.08 ± 0.41 | 16.78 ± 0.47 |
| 55 | 22.14 ± 0.60 | 20.76 ± 0.36 | 20.18 ± 0.56 |
| 60 | 30.07 ± 0.73 | 28.20 ± 0.54 | 27.16 ± 0.89 |
| 65 | 37.94 ± 0.44 | 36.67 ± 0.33 | 36.13 ± 0.61 |
| 70 | 41.46 ± 0.31 | 41.36 ± 0.32 | 40.71 ± 0.30 |

**Table 24b.** Mean DPOAE amplitude data (in dB SPL) for the Blast Only, Interrupted Conditioning then Blast, and Continuous Conditioning then Blast Groups when $f_2$=11312 Hz. Data are listed as the mean ± standard error (n=14 animals/exposure group) for primary intensity levels of 20-70 dB SPL.

| dB | Blast Only | Interrupted Conditioning then Blast | Continuous Conditioning then Blast |
|---|---|---|---|
| 20 | -12.35 ± 0.44 | -12.33 ± 0.27 | -12.82 ± 0.41 |
| 25 | -9.06 ± 0.88 | -8.69 ± 0.70 | -10.06 ± 0.72 |
| 30 | -3.77 ± 1.16 | -2.74 ± 0.93 | -5.89 ± 1.24 |
| 35 | 1.25 ± 1.33 | 3.11 ± 0.83 | -0.45 ± 1.36 |
| 40 | 5.71 ± 1.44 | 8.33 ± 0.79 | 4.07 ± 1.56 |
| 45 | 9.72 ± 1.46 | 12.86 ± 0.75 | 8.19 ± 1.75 |
| 50 | 13.54 ± 1.46 | 16.73 ± 0.74 | 11.15 ± 2.48 |
| 55 | 19.46 ± 1.27 | 20.83 ± 0.62 | 19.27 ± 1.10 |
| 60 | 28.89 ± 0.77 | 28.90 ± 0.45 | 28.19 ± 0.93 |
| 65 | 36.71 ± 0.46 | 36.71 ± 0.42 | 36.02 ± 0.45 |
| 70 | 39.96 ± 0.29 | 40.98 ± 0.38 | 39.22 ± 0.47 |

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

## VITA

Ruth Ann Skellett was born on September 25, 1962, in Port Jervis, New York. She attended kindergarten through twelfth grade in the Port Jervis Public School System. While in high school, she served as class president and earned six varsity and four junior varsity letters for her participation in various sports. She graduated high school in June of 1980.

Her college career began in September of 1980 when she enrolled at Orange County Community College. In December of 1982, she received an associate in arts degree in Social Science. She was then accepted as a student in the Computer Engineering Department at Florida Institute of Technology (F.I.T.) in September of 1983. While at F.I.T., she received an athletic scholarship (50% of tuition and fees) to play on the Women's Varsity Softball Team. She later graduated with a bachelor of science degree in June of 1987. From there she went to Richmond, Virginia, and started graduate school at the Medical College of Virginia/Virginia Commonwealth University (M.C.V./V.C.U.) in January of 1988. Under the guidance of Drs. Alex M. Clarke and Martin L. Lenhardt, she became interested in a project involving the use of ultra-high frequency vibration to evoke auditory perception. In August of 1990, she completed the requirements for a master of science degree in Biomedical Engineering by writing and defending a thesis



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

entitled "A speech discrimination device for normal and deaf subjects."

From Richmond, she moved to Baton Rouge, Louisiana, and was enrolled in the doctoral program in the Department of Communication Sciences and Disorders at Louisiana State University. After completing the required departmental coursework, she began working in the laboratory of Dr. Richard P. Bobbin at Kresge Hearing Research Laboratory of the South to pursue her interest in auditory physiology. She first became involved in a study dealing with length changes of isolated outer hair cells in response to the application of caffeine. This work resulted in a poster presentation entitled "Caffeine-induced shortening of outer hair cells" at the 17th Midwinter Research Meeting of the Association for Research in Otolaryngology and a paper entitled "Caffeine-induced shortening of isolated outer hair cells: An osmotic mechanism of action" which was published in Hearing Research in 1995. She then became involved with experiments focussed on studying the effects of noise exposure on the auditory system. Results of this series of experiments have been presented as posters entitled "The effect of continuous moderate-level noise exposure on contralateral suppression" and "Changes in distortion product otoacoustic emissions following continuous noise exposure" at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology and "Chronic low-level noise exposure alters distortion

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

product otoacoustic emissions" and "Conditioning the auditory system with continuous vs. interrupted noise of equal acoustic energy: Is either exposure more protective?" at the 19th Midwinter Research Meeting of the Association for Research in Otolaryngology. In addition, a paper entitled "Chronic low-level noise exposure alters distortion product otoacoustic emissions" has recently been accepted for publication by Hearing Research and will be printed later in 1996.

The noise exposure experiments also formed the basis of her dissertation which is entitled "Conditioning the auditory system with continuous versus interrupted noise of equal acoustic energy: Is either exposure more protective?." Upon submission and approval of her dissertation, she will have met all of the requirements for the doctor of philosophy degree in Communication Disorders. She will be awarded her degree in Communication Disorders at the summer commencement ceremony on August 1, 1996. After graduation, she plans to remain working at Kresge as a postdoctoral fellow so that she may continue her work investigating the effects of noise on the auditory system.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

## DOCTORAL EXAMINATION AND DISSERTATION REPORT

**Candidate:** Ruth Ann Skellett

**Major Field:** Communication Disorders

**Title of Dissertation:** Conditioning the Auditory System with Continous Versus Interrupted Noise of Equal Acoustic Energy: Is Either Exposure More Protective?

**Approved:**

**Major Professor and Chairman**

**Dean of the Graduate School**

**EXAMINING COMMITTEE:**

**Date of Examination:**

06/21/96

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.